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(54) Title: NOVEL COMPOUNDS

(57) Abstract: Polypeptides and polynucleotides of the genes set forth in Table I and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing polypeptides and polynucleotides of the genes set forth in Table I in diagnostic assays.

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## Novel Compounds

### Field of Invention

This invention relates to newly identified polypeptides and polynucleotides encoding such polypeptides, to their use in diagnosis and in identifying compounds that may be agonists, antagonists that are potentially useful in therapy, and to production of such polypeptides and polynucleotides. The polynucleotides and polypeptides of the present invention also relate to proteins with signal sequences which allow them to be secreted extracellularly or membrane-associated (hereinafter often referred collectively as secreted proteins or secreted polypeptides).

### Background of the Invention

The drug discovery process is currently undergoing a fundamental revolution as it embraces "functional genomics", that is, high throughput genome- or gene-based biology. This approach as a means to identify genes and gene products as therapeutic targets is rapidly superseding earlier approaches based on "positional cloning". A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position.

Functional genomics relies heavily on high-throughput DNA sequencing technologies and the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery.

Proteins and polypeptides that are naturally secreted into blood, lymph and other body fluids, or secreted into the cellular membrane are of primary interest for pharmaceutical research and development. The reason for this interest is the relative ease to target protein therapeutics into their place of action (body fluids or the cellular membrane). The natural pathway for protein secretion into extracellular space is the endoplasmic reticulum in eukaryotes and the inner membrane in prokaryotes (Palade, 1975, *Science*, 189, 347; Milstein, Brownlee, Harrison, and Mathews, 1972, *Nature New Biol.*, 239, 117; Blobel, and Dobberstein, 1975, *J. Cell. Biol.*, 67, 835). On the other hand, there is no known natural pathway for exporting a protein from the exterior of the cells into the cytosol (with the exception of pinocytosis, a mechanism of snake venom toxin intrusion into cells). Therefore targeting protein therapeutics into cells poses extreme difficulties.

The secreted and membrane-associated proteins include but are not limited to all peptide hormones and their receptors (including but not limited to insulin, growth hormones, chemokines, cytokines, neuropeptides, integrins, kallikreins, lamins, melanins, natriuretic hormones, neuropsin, neurotrophins, pituitary hormones, pleiotropins, prostaglandins, secretogranins, selectins, thromboglobulins, thymosins), the breast and colon cancer gene products, leptin, the obesity gene protein and its receptors, serum albumin, superoxide dismutase, spliceosome proteins, 7TM (transmembrane) proteins also called as G-protein coupled receptors, immunoglobulins, several families of serine proteinases (including but not limited to proteins of the blood coagulation cascade, digestive enzymes), deoxyribonuclease I, etc.

Therapeutics based on secreted or membrane-associated proteins approved by FDA or foreign agencies include but are not limited to insulin, glucagon, growth hormone, chorionic gonadotropin, follicle stimulating hormone, luteinizing hormone, calcitonin, adrenocorticotrophic hormone (ACTH), vasopressin, interleukines, interferones, immunoglobulins, lactoferrin (diverse products marketed by several companies), tissue-type plasminogen activator (Alteplase by Genentech), hyaluronidase (Wydase by Wyeth-Ayerst), dornase alpha (Pulmozyme by Genentech), Chymodiactin (chymopapain by Knoll), alglucerase (Ceredase by Genzyme), streptokinase (Kabikinase by Pharmacia) (Streptase by Astra), etc. This indicates that secreted and membrane-associated proteins have an established, proven history as therapeutic targets. Clearly, there is a need for identification and characterization of further secreted and membrane-associated proteins which can play a role in preventing, ameliorating or correcting dysfunction or disease, including but not limited to diabetes, breast-, prostate-, colon cancer and other malignant tumors, hyper- and hypotension, obesity, bulimia, anorexia, growth abnormalities, asthma, manic depression, dementia, delirium, mental retardation, Huntington's disease, Tourette's syndrome, schizophrenia, growth, mental or sexual development disorders, and dysfunctions of the blood cascade system including those leading to stroke. The proteins of the present invention which include the signal sequences are also useful to further elucidate the mechanism of protein transport which at present is not entirely understood, and thus can be used as research tools.

### Summary of the Invention

The present invention relates to particular polypeptides and polynucleotides of the genes set forth in Table I, including recombinant materials and methods for their production. Such polypeptides and polynucleotides are of interest in relation to methods of treatment of certain diseases, including, but not limited to, the diseases set forth in Tables III and V, hereinafter referred to as "diseases of the invention". In a further aspect, the invention relates to methods for identifying agonists and antagonists (*e.g.*, inhibitors) using the materials provided by the invention, and treating conditions associated with imbalance of polypeptides and/or polynucleotides of the genes set forth in Table I with the identified compounds. In still a further aspect, the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels the genes set forth in Table I. Another aspect of the invention concerns a polynucleotide comprising any of the nucleotide sequences set forth in the Sequence Listing and a polypeptide comprising a polypeptide encoded by the nucleotide sequence. In another aspect, the invention relates to a polypeptide comprising any of the polypeptide sequences set forth in the Sequence Listing and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such polypeptides and polynucleotides. Such uses include the treatment of diseases, abnormalities and disorders (hereinafter simply referred to as diseases) caused by abnormal expression, production, function and or metabolism of the genes of this invention, and such diseases are readily apparent by those skilled in the art from the homology to other proteins disclosed for each attached sequence. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with the imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the secreted proteins of the present invention.

### **Description of the Invention**

In a first aspect, the present invention relates to polypeptides the genes set forth in Table I. Such polypeptides include:

- (a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in the Sequence Listing, herein when referring to polynucleotides or polypeptides of the Sequence Listing, a reference is also made to the Sequence Listing referred to in the Sequence Listing;
- (b) an isolated polypeptide comprising a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;



- (c) an isolated polypeptide comprising a polypeptide sequence set forth in the Sequence Listing;
- (d) an isolated polypeptide having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- 5 (e) a polypeptide sequence set forth in the Sequence Listing; and
- (f) an isolated polypeptide having or comprising a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing;
- (g) fragments and variants of such polypeptides in (a) to (f).
- 10 Polypeptides of the present invention are believed to be members of the gene families set forth in Table II. They are therefore of therapeutic and diagnostic interest for the reasons set forth in Tables III and V. The biological properties of the polypeptides and polynucleotides of the genes set forth in Table I are hereinafter referred to as "the biological activity" of polypeptides and polynucleotides of the genes set forth in Table I. Preferably, a
- 15 polypeptide of the present invention exhibits at least one biological activity of the genes set forth in Table I.

Polypeptides of the present invention also include variants of the aforementioned polypeptides, including all allelic forms and splice variants. Such polypeptides vary from the reference polypeptide by insertions, deletions, and substitutions that may be

20 conservative or non-conservative, or any combination thereof. Particularly preferred variants are those in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acids are inserted, substituted, or deleted, in any combination.

Preferred fragments of polypeptides of the present invention include an isolated

25 polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids from an amino acid sequence set forth in the Sequence Listing, or an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids truncated or deleted from an amino acid sequence set forth in the Sequence Listing. Preferred fragments are biologically active fragments that mediate the biological

30 activity of polypeptides and polynucleotides of the genes set forth in Table I, including those with a similar activity or an improved activity, or with a decreased undesirable activity. Also preferred are those fragments that are antigenic or immunogenic in an animal, especially in a human.

Fragments of a polypeptide of the invention may be employed for producing the

35 corresponding full-length polypeptide by peptide synthesis; therefore, these variants may be

employed as intermediates for producing the full-length polypeptides of the invention. A polypeptide of the present invention may be in the form of the "mature" protein or may be a part of a larger protein such as a precursor or a fusion protein. It is often advantageous to include an additional amino acid sequence that contains secretory or leader sequences, pro-sequences, sequences that aid in purification, for instance multiple histidine residues, or an additional sequence for stability during recombinant production.

Polypeptides of the present invention can be prepared in any suitable manner, for instance by isolation from naturally occurring sources, from genetically engineered host cells comprising expression systems (*vide infra*) or by chemical synthesis, using for instance automated peptide synthesizers, or a combination of such methods. Means for preparing such polypeptides are well understood in the art.

In a further aspect, the present invention relates to polynucleotides of the genes set forth in Table I. Such polynucleotides include:

- (a) an isolated polynucleotide comprising a polynucleotide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide sequence set forth in the Sequence Listing;
- (b) an isolated polynucleotide comprising a polynucleotide set forth in the Sequence Listing;
- (c) an isolated polynucleotide having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide set forth in the Sequence Listing;
- (d) an isolated polynucleotide set forth in the Sequence Listing;
- (e) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- (f) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing;
- (g) an isolated polynucleotide having a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- (h) an isolated polynucleotide encoding a polypeptide set forth in the Sequence Listing;
- (i) an isolated polynucleotide having or comprising a polynucleotide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polynucleotide sequence set forth in the Sequence Listing;

(j) an isolated polynucleotide having or comprising a polynucleotide sequence encoding a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing; and polynucleotides that are fragments and variants of the above mentioned polynucleotides or that are complementary to above mentioned polynucleotides, over the entire length thereof.

Preferred fragments of polynucleotides of the present invention include an isolated polynucleotide comprising a nucleotide sequence having at least 15, 30, 50 or 100 contiguous nucleotides from a sequence set forth in the Sequence Listing, or an isolated polynucleotide comprising a sequence having at least 30, 50 or 100 contiguous nucleotides truncated or deleted from a sequence set forth in the Sequence Listing.

Preferred variants of polynucleotides of the present invention include splice variants, allelic variants, and polymorphisms, including polynucleotides having one or more single nucleotide polymorphisms (SNPs).

Polynucleotides of the present invention also include polynucleotides encoding polypeptide variants that comprise an amino acid sequence set forth in the Sequence Listing and in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acid residues are substituted, deleted or added, in any combination.

In a further aspect, the present invention provides polynucleotides that are RNA transcripts of the DNA sequences of the present invention. Accordingly, there is provided an RNA polynucleotide that:

(a) comprises an RNA transcript of the DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(b) is a RNA transcript of a DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(c) comprises an RNA transcript of a DNA sequence set forth in the Sequence Listing; or

(d) is a RNA transcript of a DNA sequence set forth in the Sequence Listing; and RNA polynucleotides that are complementary thereto.

The polynucleotide sequences set forth in the Sequence Listing show homology with the polynucleotide sequences set forth in Table II. A polynucleotide sequence set forth in the Sequence Listing is a cDNA sequence that encodes a polypeptide set forth in the Sequence Listing. A polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing may be identical to a polypeptide encoding a sequence set forth in the Sequence Listing or it may be a sequence other than a sequence set forth in the Sequence

Listing, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes a polypeptide set forth in the Sequence Listing. A polypeptide of a sequence set forth in the Sequence Listing is related to other proteins of the gene families set forth in Table II, having homology and/or structural similarity with the polypeptides set forth in Table II. Preferred  
5 polypeptides and polynucleotides of the present invention are expected to have, *inter alia*, similar biological functions/properties to their homologous polypeptides and polynucleotides. Furthermore, preferred polypeptides and polynucleotides of the present invention have at least one activity of the genes set forth in Table I.

Polynucleotides of the present invention may be obtained using standard cloning  
10 and screening techniques from a cDNA library derived from mRNA from the tissues set forth in Table IV (see for instance, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries or can be synthesized using well known and commercially available  
15 techniques.

When polynucleotides of the present invention are used for the recombinant production of polypeptides of the present invention, the polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader  
20 or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain preferred embodiments of this aspect of the invention, the marker sequence is a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, Proc Natl Acad Sci USA (1989) 86:821-824, or  
25 is an HA tag. A polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals, ribosome binding sites and sequences that stabilize mRNA.

Polynucleotides that are identical, or have sufficient identity to a polynucleotide sequence set forth in the Sequence Listing, may be used as hybridization probes for cDNA  
30 and genomic DNA or as primers for a nucleic acid amplification reaction (for instance, PCR). Such probes and primers may be used to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding paralogs from human sources and orthologs and paralogs from other species) that have a high sequence similarity to sequences set forth  
35 in the Sequence Listing, typically at least 95% identity. Preferred probes and primers will

generally comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50, if not at least 100 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides. Particularly preferred primers will have between 20 and 25 nucleotides.

5           A polynucleotide encoding a polypeptide of the present invention, including homologs from other species, may be obtained by a process comprising the steps of screening a library under stringent hybridization conditions with a labeled probe having a sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides; and isolating full-length cDNA and genomic clones containing the  
10 polynucleotide sequence set forth in the Sequence Listing. Such hybridization techniques are well known to the skilled artisan. Preferred stringent hybridization conditions include overnight incubation at 42°C in a solution comprising: 50% formamide, 5xSSC (150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10 % dextran sulfate, and 20 microgram/ml denatured, sheared salmon sperm DNA;  
15 followed by washing the filters in 0.1x SSC at about 65°C. Thus the present invention also includes isolated polynucleotides, preferably with a nucleotide sequence of at least 100, obtained by screening a library under stringent hybridization conditions with a labeled probe having the sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides.

20           The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for the polypeptide does not extend all the way through to the 5' terminus. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerisation reaction), failing to complete a DNA copy of the  
25 mRNA template during first strand cDNA synthesis.

          There are several methods available and well known to those skilled in the art to obtain full-length cDNAs, or extend short cDNAs, for example those based on the method of Rapid Amplification of cDNA ends (RACE) (see, for example, Frohman et al., Proc Nat Acad Sci USA 85, 8998-9002, 1988). Recent modifications of the technique, exemplified  
30 by the Marathon (trade mark) technology (Clontech Laboratories Inc.) for example, have significantly simplified the search for longer cDNAs. In the Marathon (trade mark) technology, cDNAs have been prepared from mRNA extracted from a chosen tissue and an 'adaptor' sequence ligated onto each end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5' end of the cDNA using a combination of gene specific and  
35 adaptor specific oligonucleotide primers. The PCR reaction is then repeated using 'nested'

primers, that is, primers designed to anneal within the amplified product (typically an adapter specific primer that anneals further 3' in the adaptor sequence and a gene specific primer that anneals further 5' in the known gene sequence). The products of this reaction can then be analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

Recombinant polypeptides of the present invention may be prepared by processes well known in the art from genetically engineered host cells comprising expression systems. Accordingly, in a further aspect, the present invention relates to expression systems comprising a polynucleotide or polynucleotides of the present invention, to host cells which are genetically engineered with such expression systems and to the production of polypeptides of the invention by recombinant techniques. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention.

For recombinant production, host cells can be genetically engineered to incorporate expression systems or portions thereof for polynucleotides of the present invention. Polynucleotides may be introduced into host cells by methods described in many standard laboratory manuals, such as Davis et al., Basic Methods in Molecular Biology (1986) and Sambrook *et al.* (*ibid*). Preferred methods of introducing polynucleotides into host cells include, for instance, calcium phosphate transfection, DEAE-dextran mediated transfection, transvection, micro-injection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction or infection.

Representative examples of appropriate hosts include bacterial cells, such as *Streptococci*, *Staphylococci*, *E. coli*, *Streptomyces* and *Bacillus subtilis* cells; fungal cells, such as yeast cells and *Aspergillus* cells; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, HEK 293 and Bowes melanoma cells; and plant cells.

A great variety of expression systems can be used, for instance, chromosomal, episomal and virus-derived systems, *e.g.*, vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids. The expression systems

may contain control regions that regulate as well as engender expression. Generally, any system or vector that is able to maintain, propagate or express a polynucleotide to produce a polypeptide in a host may be used. The appropriate polynucleotide sequence may be inserted into an expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook *et al.*, (*ibid*). Appropriate secretion signals may be incorporated into the desired polypeptide to allow secretion of the translated protein into the lumen of the endoplasmic reticulum, the periplasmic space or the extracellular environment. These signals may be endogenous to the polypeptide or they may be heterologous signals.

10 If a polypeptide of the present invention is to be expressed for use in screening assays, it is generally preferred that the polypeptide be produced at the surface of the cell. In this event, the cells may be harvested prior to use in the screening assay. If the polypeptide is secreted into the medium, the medium can be recovered in order to recover and purify the polypeptide. If produced intracellularly, the cells must first be lysed before  
15 the polypeptide is recovered.

Polypeptides of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography,  
20 hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation and/or purification.

Polynucleotides of the present invention may be used as diagnostic reagents,  
25 through detecting mutations in the associated gene. Detection of a mutated form of a gene is characterized by the polynucleotides set forth in the Sequence Listing in the cDNA or genomic sequence and which is associated with a dysfunction. Will provide a diagnostic tool that can add to, or define, a diagnosis of a disease, or susceptibility to a disease, which results from under-expression, over-expression or altered spatial or temporal expression of the gene. Individuals carrying mutations in the gene may be detected at the DNA level by a  
30 variety of techniques well known in the art.

Nucleic acids for diagnosis may be obtained from a subject's cells, such as from blood, urine, saliva, tissue biopsy or autopsy material. The genomic DNA may be used directly for detection or it may be amplified enzymatically by using PCR, preferably RT-  
35 PCR, or other amplification techniques prior to analysis. RNA or cDNA may also be used

in similar fashion. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to labeled nucleotide sequences of the genes set forth in Table I. Perfectly matched sequences can be distinguished from mismatched duplexes by  
5 RNase digestion or by differences in melting temperatures. DNA sequence difference may also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agents, or by direct DNA sequencing (see, for instance, Myers *et al.*, Science (1985) 230:1242). Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the chemical cleavage  
10 method (see Cotton *et al.*, Proc Natl Acad Sci USA (1985) 85: 4397-4401).

An array of oligonucleotides probes comprising polynucleotide sequences or fragments thereof of the genes set forth in Table I can be constructed to conduct efficient screening of *e.g.*, genetic mutations. Such arrays are preferably high density arrays or grids. Array technology methods are well known and have general applicability and can be used to  
15 address a variety of questions in molecular genetics including gene expression, genetic linkage, and genetic variability, see, for example, M. Chee *et al.*, Science, 274, 610-613 (1996) and other references cited therein.

Detection of abnormally decreased or increased levels of polypeptide or mRNA expression may also be used for diagnosing or determining susceptibility of a subject to a disease of the invention. Decreased or increased expression can be measured at the RNA level using any  
20 of the methods well known in the art for the quantitation of polynucleotides, such as, for example, nucleic acid amplification, for instance PCR, RT-PCR, RNase protection, Northern blotting and other hybridization methods. Assay techniques that can be used to determine levels of a protein, such as a polypeptide of the present invention, in a sample  
25 derived from a host are well-known to those of skill in the art. Such assay methods include radio-immunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

Thus in another aspect, the present invention relates to a diagnostic kit comprising:  
(a) a polynucleotide of the present invention, preferably the nucleotide sequence set forth in the Sequence Listing, or a fragment or an RNA transcript thereof;  
30 (b) a nucleotide sequence complementary to that of (a);  
(c) a polypeptide of the present invention, preferably the polypeptide set forth in the Sequence Listing or a fragment thereof; or  
(d) an antibody to a polypeptide of the present invention, preferably to the polypeptide set forth in the Sequence Listing.



It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component. Such a kit will be of use in diagnosing a disease or susceptibility to a disease, particularly diseases of the invention, amongst others.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequences set forth in the Sequence Listing are specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an important first step in correlating those sequences with gene associated disease. Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillett, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, *Nature Genetics* 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (*Hum Mol Genet* 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillett D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. This comparison is conducted at <http://www.genome.wi.mit.edu/>.

The polynucleotide sequences of the present invention are also valuable tools for tissue expression studies. Such studies allow the determination of expression patterns of polynucleotides of the present invention which may give an indication as to the expression patterns of the encoded polypeptides in tissues, by detecting the mRNAs that encode them. The techniques used are well known in the art and include in situ hybridization techniques to clones arrayed on a grid, such as cDNA microarray hybridization (Schena *et al*, *Science*,

270, 467-470, 1995 and Shalon *et al.*, Genome Res, 6, 639-645, 1996) and nucleotide amplification techniques such as PCR. A preferred method uses the TAQMAN (Trade mark) technology available from Perkin Elmer. Results from these studies can provide an indication of the normal function of the polypeptide in the organism. In addition,

5 comparative studies of the normal expression pattern of mRNAs with that of mRNAs encoded by an alternative form of the same gene (for example, one having an alteration in polypeptide coding potential or a regulatory mutation) can provide valuable insights into the role of the polypeptides of the present invention, or that of inappropriate expression thereof in disease. Such inappropriate expression may be of a temporal, spatial or simply  
10 quantitative nature.

A further aspect of the present invention relates to antibodies. The polypeptides of the invention or their fragments, or cells expressing them, can be used as immunogens to produce antibodies that are immunospecific for polypeptides of the present invention. The term "immunospecific" means that the antibodies have substantially greater affinity for the  
15 polypeptides of the invention than their affinity for other related polypeptides in the prior art.

Antibodies generated against polypeptides of the present invention may be obtained by administering the polypeptides or epitope-bearing fragments, or cells to an animal, preferably a non-human animal, using routine protocols. For preparation of monoclonal  
20 antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler, G. and Milstein, C., Nature (1975) 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al.*, Immunology Today (1983) 4:72) and the EBV-hybridoma technique (Cole *et al.*, Monoclonal Antibodies and Cancer Therapy, 77-96, Alan R. Liss,  
25 Inc., 1985).

Techniques for the production of single chain antibodies, such as those described in U.S. Patent No. 4,946,778, can also be adapted to produce single chain antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms, including other mammals, may be used to express humanized antibodies.

30 The above-described antibodies may be employed to isolate or to identify clones expressing the polypeptide or to purify the polypeptides by affinity chromatography. Antibodies against polypeptides of the present invention may also be employed to treat diseases of the invention, amongst others.

Polypeptides and polynucleotides of the present invention may also be used as  
35 vaccines. Accordingly, in a further aspect, the present invention relates to a method for

inducing an immunological response in a mammal that comprises inoculating the mammal with a polypeptide of the present invention, adequate to produce antibody and/or T cell immune response, including, for example, cytokine-producing T cells or cytotoxic T cells, to protect said animal from disease, whether that disease is already established within the individual or not. An immunological response in a mammal may also be induced by a method comprises delivering a polypeptide of the present invention *via* a vector directing expression of the polynucleotide and coding for the polypeptide *in vivo* in order to induce such an immunological response to produce antibody to protect said animal from diseases of the invention. One way of administering the vector is by accelerating it into the desired cells as a coating on particles or otherwise. Such nucleic acid vector may comprise DNA, RNA, a modified nucleic acid, or a DNA/RNA hybrid. For use a vaccine, a polypeptide or a nucleic acid vector will be normally provided as a vaccine formulation (composition). The formulation may further comprise a suitable carrier. Since a polypeptide may be broken down in the stomach, it is preferably administered parenterally (for instance, subcutaneous, intra-muscular, intravenous, or intra-dermal injection). Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions that may contain anti-oxidants, buffers, bacteriostats and solutes that render the formulation isotonic with the blood of the recipient; and aqueous and non-aqueous sterile suspensions that may include suspending agents or thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example, sealed ampoules and vials and may be stored in a freeze-dried condition requiring only the addition of the sterile liquid carrier immediately prior to use. The vaccine formulation may also include adjuvant systems for enhancing the immunogenicity of the formulation, such as oil-in water systems and other systems known in the art. The dosage will depend on the specific activity of the vaccine and can be readily determined by routine experimentation.

Polypeptides of the present invention have one or more biological functions that are of relevance in one or more disease states, in particular the diseases of the invention hereinbefore mentioned. It is therefore useful to identify compounds that stimulate or inhibit the function or level of the polypeptide. Accordingly, in a further aspect, the present invention provides for a method of screening compounds to identify those that stimulate or inhibit the function or level of the polypeptide. Such methods identify agonists or antagonists that may be employed for therapeutic and prophylactic purposes for such diseases of the invention as hereinbefore mentioned. Compounds may be identified from a variety of sources, for example, cells, cell-free preparations, chemical libraries, collections of chemical compounds, and natural product mixtures. Such agonists or antagonists so-

identified may be natural or modified substrates, ligands, receptors, enzymes, etc., as the case may be, of the polypeptide; a structural or functional mimetic thereof (see Coligan *et al.*, Current Protocols in Immunology 1(2):Chapter 5 (1991)) or a small molecule. Such small molecules preferably have a molecular weight below 2,000 daltons, more preferably  
5 between 300 and 1,000 daltons, and most preferably between 400 and 700 daltons. It is preferred that these small molecules are organic molecules.

The screening method may simply measure the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide, or a fusion protein thereof, by means of a label directly or indirectly associated with the candidate compound.  
10 Alternatively, the screening method may involve measuring or detecting (qualitatively or quantitatively) the competitive binding of a candidate compound to the polypeptide against a labeled competitor (*e.g.* agonist or antagonist). Further, these screening methods may test whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells bearing the polypeptide.  
15 Inhibitors of activation are generally assayed in the presence of a known agonist and the effect on activation by the agonist by the presence of the candidate compound is observed. Further, the screening methods may simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide of the present invention, to form a mixture, measuring an activity of the genes set forth in Table I in the mixture, and  
20 comparing activity of the mixture of the genes set forth in Table I to a control mixture which contains no candidate compound.

Polypeptides of the present invention may be employed in conventional low capacity screening methods and also in high-throughput screening (HTS) formats. Such HTS formats include not only the well-established use of 96- and, more recently, 384-well  
25 micotiter plates but also emerging methods such as the nanowell method described by Schullek *et al.*, Anal Biochem., 246, 20-29, (1997).

Fusion proteins, such as those made from Fc portion and polypeptide of the genes set forth in Table I, as hereinbefore described, can also be used for high-throughput screening assays to identify antagonists for the polypeptide of the present invention (see D. Bennett *et al.*, J  
30 Mol Recognition, 8:52-58 (1995); and K. Johanson *et al.*, J Biol Chem, 270(16):9459-9471 (1995)).

The polynucleotides, polypeptides and antibodies to the polypeptide of the present invention may also be used to configure screening methods for detecting the effect of added compounds on the production of mRNA and polypeptide in cells. For example, an ELISA  
35 assay may be constructed for measuring secreted or cell associated levels of polypeptide

using monoclonal and polyclonal antibodies by standard methods known in the art. This can be used to discover agents that may inhibit or enhance the production of polypeptide (also called antagonist or agonist, respectively) from suitably manipulated cells or tissues.

5 A polypeptide of the present invention may be used to identify membrane bound or soluble receptors, if any, through standard receptor binding techniques known in the art. These include, but are not limited to, ligand binding and crosslinking assays in which the polypeptide is labeled with a radioactive isotope (for instance,  $^{125}\text{I}$ ), chemically modified (for instance, biotinylated), or fused to a peptide sequence suitable for detection or purification, and incubated with a source of the putative receptor (cells, cell membranes, cell  
10 supernatants, tissue extracts, bodily fluids). Other methods include biophysical techniques such as surface plasmon resonance and spectroscopy. These screening methods may also be used to identify agonists and antagonists of the polypeptide that compete with the binding of the polypeptide to its receptors, if any. Standard methods for conducting such assays are well understood in the art.

15 Examples of antagonists of polypeptides of the present invention include antibodies or, in some cases, oligonucleotides or proteins that are closely related to the ligands, substrates, receptors, enzymes, etc., as the case may be, of the polypeptide, *e.g.*, a fragment of the ligands, substrates, receptors, enzymes, etc.; or a small molecule that bind to the polypeptide of the present invention but do not elicit a response, so that the activity of the  
20 polypeptide is prevented.

Screening methods may also involve the use of transgenic technology and the genes set forth in Table I. The art of constructing transgenic animals is well established. For example, the genes set forth in Table I may be introduced through microinjection into the male pronucleus of fertilized oocytes, retroviral transfer into pre- or post-implantation  
25 embryos, or injection of genetically modified, such as by electroporation, embryonic stem cells into host blastocysts. Particularly useful transgenic animals are so-called "knock-in" animals in which an animal gene is replaced by the human equivalent within the genome of that animal. Knock-in transgenic animals are useful in the drug discovery process, for target validation, where the compound is specific for the human target. Other useful transgenic  
30 animals are so-called "knock-out" animals in which the expression of the animal ortholog of a polypeptide of the present invention and encoded by an endogenous DNA sequence in a cell is partially or completely annulled. The gene knock-out may be targeted to specific cells or tissues, may occur only in certain cells or tissues as a consequence of the limitations of the technology, or may occur in all, or substantially all, cells in the animal. Transgenic  
35 animal technology also offers a whole animal expression-cloning system in which

introduced genes are expressed to give large amounts of polypeptides of the present invention

Screening kits for use in the above described methods form a further aspect of the present invention. Such screening kits comprise:

- 5 (a) a polypeptide of the present invention;  
(b) a recombinant cell expressing a polypeptide of the present invention;  
(c) a cell membrane expressing a polypeptide of the present invention; or  
(d) an antibody to a polypeptide of the present invention;

which polypeptide is preferably that set forth in the Sequence Listing.

- 10 It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component.

### Glossary

- The following definitions are provided to facilitate understanding of certain terms used frequently hereinbefore.

"Antibodies" as used herein includes polyclonal and monoclonal antibodies, chimeric, single chain, and humanized antibodies, as well as Fab fragments, including the products of an

Fab or other immunoglobulin expression library.

- 20 "Isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated", as the term is employed herein. Moreover, a  
25 polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method is "isolated" even if it is still present in said organism, which organism may be living or non-living.

- "Secreted protein activity or secreted polypeptide activity" or "biological activity of the secreted protein or secreted polypeptide" refers to the metabolic or physiologic function  
30 of said secreted protein including similar activities or improved activities or these activities with decreased undesirable side-effects. Also included are antigenic and immunogenic activities of said secreted protein.

"Secreted protein gene" refers to a polynucleotide comprising any of the attached nucleotide sequences or allelic variants thereof and/or their complements.

"Polynucleotide" generally refers to any polyribonucleotide (RNA) or polydeoxribonucleotide (DNA), which may be unmodified or modified RNA or DNA.

"Polynucleotides" include, without limitation, single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term "polynucleotide" also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications may be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" also embraces relatively short polynucleotides, often referred to as oligonucleotides.

"Polypeptide" refers to any polypeptide comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres. "Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. Polypeptides may contain amino acids other than the 20 gene-encoded amino acids. "Polypeptides" include amino acid sequences modified either by natural processes, such as post-translational processing, or by chemical modification techniques that are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications may occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present to the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched and branched cyclic polypeptides may result from post-translation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, biotinylation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-

linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation,

5 racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination (see, for instance, *Proteins - Structure and Molecular Properties*, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York, 1993; Wold, F., *Post-translational Protein Modifications: Perspectives and Prospects*, 1-12, in *Post-translational Covalent Modification of Proteins*, B. C. Johnson, Ed., Academic Press,

10 New York, 1983; Seifter *et al.*, "Analysis for protein modifications and nonprotein cofactors", *Meth Enzymol*, 182, 626-646, 1990, and Rattan *et al.*, "Protein Synthesis: Post-translational Modifications and Aging", *Ann NY Acad Sci*, 663, 48-62, 1992).

"Fragment" of a polypeptide sequence refers to a polypeptide sequence that is shorter than the reference sequence but that retains essentially the same biological function

15 or activity as the reference polypeptide. "Fragment" of a polynucleotide sequence refers to a polynucleotide sequence that is shorter than the reference sequence set forth in the Sequence Listing.

"Variant" refers to a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide, but retains the essential properties thereof. A typical variant

20 of a polynucleotide differs in nucleotide sequence from the reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference sequence, as discussed below. A typical variant of a

25 polypeptide differs in amino acid sequence from the reference polypeptide. Generally, alterations are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid sequence by one or more substitutions, insertions, deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded

30 by the genetic code. Typical conservative substitutions include Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe and Tyr. A variant of a polynucleotide or polypeptide may be naturally occurring such as an allele, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides may be made by mutagenesis techniques or by direct synthesis. Also included

35 as variants are polypeptides having one or more post-translational modifications, for



instance glycosylation, phosphorylation, methylation, ADP ribosylation and the like. Embodiments include methylation of the N-terminal amino acid, phosphorylations of serines and threonines and modification of C-terminal glycines.

5 "Allele" refers to one of two or more alternative forms of a gene occurring at a given locus in the genome.

"Polymorphism" refers to a variation in nucleotide sequence (and encoded polypeptide sequence, if relevant) at a given position in the genome within a population.

10 "Single Nucleotide Polymorphism" (SNP) refers to the occurrence of nucleotide variability at a single nucleotide position in the genome, within a population. An SNP may occur within a gene or within intergenic regions of the genome. SNPs can be assayed using Allele Specific Amplification (ASA). For the process at least 3 primers are required. A common primer is used in reverse complement to the polymorphism being assayed. This common primer can be between 50 and 1500 bps from the polymorphic base. The other two (or more) primers are identical to each other except that the final 3' base wobbles to match one of the two (or more) alleles that make up the polymorphism. Two (or more) PCR reactions are then conducted on sample DNA, each using the common primer and one of the Allele Specific Primers.

20 "Splice Variant" as used herein refers to cDNA molecules produced from RNA molecules initially transcribed from the same genomic DNA sequence but which have undergone alternative RNA splicing. Alternative RNA splicing occurs when a primary RNA transcript undergoes splicing, generally for the removal of introns, which results in the production of more than one mRNA molecule each of that may encode different amino acid sequences. The term splice variant also refers to the proteins encoded by the above cDNA molecules.

25 "Identity" reflects a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, determined by comparing the sequences. In general, identity refers to an exact nucleotide to nucleotide or amino acid to amino acid correspondence of the two polynucleotide or two polypeptide sequences, respectively, over the length of the sequences being compared.

30 "% Identity" - For sequences where there is not an exact correspondence, a "% identity" may be determined. In general, the two sequences to be compared are aligned to give a maximum correlation between the sequences. This may include inserting "gaps" in either one or both sequences, to enhance the degree of alignment. A % identity may be determined over the whole length of each of the sequences being compared (so-called global alignment), that is particularly suitable for sequences of the same or very similar length, or

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over shorter, defined lengths (so-called local alignment), that is more suitable for sequences of unequal length.

"Similarity" is a further, more sophisticated measure of the relationship between two polypeptide sequences. In general, "similarity" means a comparison between the amino acids of two polypeptide chains, on a residue by residue basis, taking into account not only exact correspondences between a between pairs of residues, one from each of the sequences being compared (as for identity) but also, where there is not an exact correspondence, whether, on an evolutionary basis, one residue is a likely substitute for the other. This likelihood has an associated "score" from which the "% similarity" of the two sequences can then be determined.

Methods for comparing the identity and similarity of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux J et al, Nucleic Acids Res, 12, 387-395, 1984, available from Genetics Computer Group, Madison, Wisconsin, USA), for example the programs BESTFIT and GAP, may be used to determine the % identity between two polynucleotides and the % identity and the % similarity between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (J Mol Biol, 147,195-197, 1981, Advances in Applied Mathematics, 2, 482-489, 1981) and finds the best single region of similarity between two sequences. BESTFIT is more suited to comparing two polynucleotide or two polypeptide sequences that are dissimilar in length, the program assuming that the shorter sequence represents a portion of the longer. In comparison, GAP aligns two sequences, finding a "maximum similarity", according to the algorithm of Neddleman and Wunsch (J Mol Biol, 48, 443-453, 1970). GAP is more suited to comparing sequences that are approximately the same length and an alignment is expected over the entire length. Preferably, the parameters "Gap Weight" and "Length Weight" used in each program are 50 and 3, for polynucleotide sequences and 12 and 4 for polypeptide sequences, respectively. Preferably, % identities and similarities are determined when the two sequences being compared are optimally aligned.

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215, 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99,

1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448, 1988, available as part of the Wisconsin Sequence Analysis Package).

Preferably, the BLOSUM62 amino acid substitution matrix (Henikoff S and Henikoff J G, Proc. Nat. Acad Sci. USA, 89, 10915-10919, 1992) is used in polypeptide sequence comparisons including where nucleotide sequences are first translated into amino acid sequences before comparison.

Preferably, the program BESTFIT is used to determine the % identity of a query polynucleotide or a polypeptide sequence with respect to a reference polynucleotide or a polypeptide sequence, the query and the reference sequence being optimally aligned and the parameters of the program set at the default value, as hereinbefore described.

"Identity Index" is a measure of sequence relatedness which may be used to compare a candidate sequence (polynucleotide or polypeptide) and a reference sequence. Thus, for instance, a candidate polynucleotide sequence having, for example, an Identity Index of 0.95 compared to a reference polynucleotide sequence is identical to the reference sequence except that the candidate polynucleotide sequence may include on average up to five differences per each 100 nucleotides of the reference sequence. Such differences are selected from the group consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion. These differences may occur at the 5' or 3' terminal positions of the reference polynucleotide sequence or anywhere between these terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polynucleotide sequence having an Identity Index of 0.95 compared to a reference polynucleotide sequence, an average of up to 5 in every 100 of the nucleotides of the in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

Similarly, for a polypeptide, a candidate polypeptide sequence having, for example, an Identity Index of 0.95 compared to a reference polypeptide sequence is identical to the reference sequence except that the polypeptide sequence may include an average of up to five differences per each 100 amino acids of the reference sequence. Such differences are selected from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion. These differences may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between these terminal positions, interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups

within the reference sequence. In other words, to obtain a polypeptide sequence having an Identity Index of 0.95 compared to a reference polypeptide sequence, an average of up to 5 in every 100 of the amino acids in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis*  
 5 *mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

The relationship between the number of nucleotide or amino acid differences and the Identity Index may be expressed in the following equation:

$$n_a \leq x_a - (x_a \cdot I),$$

in which:

- 10  $n_a$  is the number of nucleotide or amino acid differences,  
 $x_a$  is the total number of nucleotides or amino acids in a sequence set forth in the Sequence Listing,  
 I is the Identity Index,  
 • is the symbol for the multiplication operator, and  
 15 in which any non-integer product of  $x_a$  and I is rounded down to the nearest integer prior to subtracting it from  $x_a$ .

"Homolog" is a generic term used in the art to indicate a polynucleotide or polypeptide sequence possessing a high degree of sequence relatedness to a reference sequence. Such relatedness may be quantified by determining the degree of identity and/or  
 20 similarity between the two sequences as hereinbefore defined. Falling within this generic term are the terms "ortholog", and "paralog". "Ortholog" refers to a polynucleotide or polypeptide that is the functional equivalent of the polynucleotide or polypeptide in another species. "Paralog" refers to a polynucleotide or polypeptide that within the same species which is functionally similar.

25 "Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. In one example, EP-A-0 464 533-A discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for  
 30 example, improved pharmacokinetic properties [see, *e.g.*, EP-A 0232 262]. On the other hand, for some uses it would be desirable to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

All publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety  
 35 as if each individual publication or reference were specifically and individually indicated to

be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in its entirety in the manner described above for publications and references.

**Table I.**

Gene Name	GSK Gene ID	Nucleic Acid SEQ ID NO's	Corresponding Protein SEQ ID NO's
sbg318680DNase	318680	SEQ ID NO:1	SEQ ID NO:40
sbg237038SA	237038	SEQ ID NO:2 SEQ ID NO:3	SEQ ID NO:41 SEQ ID NO:42
sbg340871GPV	340871	SEQ ID NO:4	SEQ ID NO:43
sbg293416HNKS	293416	SEQ ID NO:5 SEQ ID NO:6	SEQ ID NO:44 SEQ ID NO:45
sbg257418ZP	257418	SEQ ID NO:7	SEQ ID NO:46
sbg319185CDa	319185	SEQ ID NO:8 SEQ ID NO:9	SEQ ID NO:47 SEQ ID NO:48
sbg323307KIAAa	323307	SEQ ID NO:10	SEQ ID NO:49
sbg315953GPPa	315953	SEQ ID NO:11 SEQ ID NO:12	SEQ ID NO:50 SEQ ID NO:51
sbg318486ONC	318486	SEQ ID NO:13	SEQ ID NO:52
sbg299359LIPO	299359	SEQ ID NO:14	SEQ ID NO:53
sbg230022NGa	230022	SEQ ID NO:15 SEQ ID NO:16	SEQ ID NO:54 SEQ ID NO:55
sbg297169BGP	297169	SEQ ID NO:17 SEQ ID NO:18	SEQ ID NO:56 SEQ ID NO:57

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sbg253919HSCCAa	253919	SEQ ID NO:19 SEQ ID NO:20	SEQ ID NO:58 SEQ ID NO:59
sbg228137OLF	228137	SEQ ID NO:21 SEQ ID NO:22	SEQ ID NO:60 SEQ ID NO:61
sbg378514Netrin	378514	SEQ ID NO:23 SEQ ID NO:24	SEQ ID NO:62 SEQ ID NO:63
sbg253227.mucous matrix glycoprotein	253227	SEQ ID NO:25 SEQ ID NO:26	SEQ ID NO:64 SEQ ID NO:65
sbg262831SIAa	262831	SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:66 SEQ ID NO:67
sbg233728LIPASE	233728	SEQ ID NO:29	SEQ ID NO:68
sbg400455.CRF	400455	SEQ ID NO:30	SEQ ID NO:69
sbg400612KINASEa	400612	SEQ ID NO:31	SEQ ID NO:70
sbg381373ACRP	381373	SEQ ID NO:32	SEQ ID NO:71
sbg401294MEX-3	401294	SEQ ID NO:33 SEQ ID NO:34	SEQ ID NO:72 SEQ ID NO:73
sbg247722Cadherin	247722	SEQ ID NO:35 SEQ ID NO:36	SEQ ID NO:74 SEQ ID NO:75
sbg391057THIPa	391057	SEQ ID NO:37 SEQ ID NO:38	SEQ ID NO:76 SEQ ID NO:77
sbg378067TGFC	378067	SEQ ID NO:39	SEQ ID NO:78

Table II

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg318680-DNase	DNase I	GB:AC022471 Submitted (04-FEB-2000) by Lita Annenberg Hazen Genome Sequencing Center, Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724, USA.	Human DNase I-like endonuclease, gi:5803007 Parrish JE, Ciccodicola A, Wehhert M, Cox GF, Chen E, and Nelson DL; 1995; Hum. Mol. Genet. 4:1557-1564.	Secreted
sbg237038-SA	SA protein	GB:AC023292 Submitted (11-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Human SA gene, gi:2988399 Loftus,B.J. et al. Genomics 60 (3), 295- 308 (1999)	Secreted
sbg340871-GPV	Platelet glycoprotein (GPV)	GB:AC025389 Submitted (08-MAR-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Rat platelet glycoprotein V (GPV) precursor, gi:6980974 Ravanat C, Morales M, Azorsa DO, Moog S, Schuhler S, Grunert P, Loew D, Van Dorsselaer A, Cazenave JP, Lanza F; 1997; Blood 89:3253-62.	Secreted
sbg293416-HNKS	HNK-1 sulfotransferase	JGI:LLNL-R_241B6 Joint Genome Institute, Department of Energy, USA	Human GalNAc 4- sulfotransferase, gi:11990885 Okuda,T., Mita,S., Yamauchi,S., Fukuta,M., Nakano,H., Sawada,T. and Habuchi,O. J. Biol. Chem. 275 (51), 40605- 40613 (2000)	Secreted
sbg257418-ZP	Zona pellucida protein	GB:AP000777 Submitted (25-NOV-1999) to the DDBJ/EMBL/GenBank databases. Masahira Hattori, The Institute of Physical and Chemical Research (RIKEN), Genomic Sciences Center (GSC); Kitasato Univ., 1- 15-1 Kitasato, Sagamihara, Kanagawa 228-8555, Japan.	Mouse zona pellucida glycoprotein, gi:6677653 Epifano,O., Liang,L.F., Familar,M., Moos,M.C. Jr. and Dean,J.; 1995; Development 121:1947- 1956.	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg319185-CDa	Leukocyte differentiation antigen	GB:AC024004 Submitted (20-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human leukocyte differentiation antigen CD84 isoform CD84s, gi:6650112 Submitted (20-MAR-1998) by Servei d'Immunologia, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain	Secreted
sbg323307-KIAAa	Slit-like	GB:AL160156, Submitted (10-MAR-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human unnamed protein, gi:10439289 Submitted (29-AUG-2000) by Sumio Sugano, Institute of Medical Science, University of Tokyo, Laboratory of Genome Structure Analysis, Human Genome Center; Shirokane-dai, 4-6-1, Minato-ku, Tokyo 108-8639, Japan	Secreted
sbg315953-GPPa	Granulocyte peptide A	GB:AC011666 Submitted (09-OCT-1999) by Department Of Chemistry And Biochemistry, The University Of Oklahoma, 620 Parrington Oval, Room 208, Norman, OK 73019, USA	Human hypothetical protein SBBI67, gi:9966869 Submitted (08-MAR-2000) by Department of Immunology, Second Military Medical University & Shanghai Brilliance Biotechnology Institute, 800 Xiangyin Rd., Shanghai 200433, P.R. China	Secreted
sbg318486-ONC	Oncotrophoblast glycoprotein	GB:AC022045 Submitted (25-JAN-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Canine 5T4 tumour-associated antigen' gene: Y94351 Submitted by OXFORD BIOMEDICA UK LTD Publication number and date: WO200029428-A2, 25-MAY-00	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg29935 9-LIPO	Lipocalin	SC:AL139041 Submitted (16-NOV-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK	Mouse major urinary protein (MUP) 4, gi:6678968 Shahan K, Gilmartin M, and Derman E; 1987; Mol Cell Biol 7:1938- 1946.	Secreted
sbg23002 2-NGa	Plasmacytoma -associated neuronal glycoprotein	GB:AC066608 GB:AC022002 Submitted (25-APR-2000) and (24-JAN-2000) by Human Genomic Center, Institute of Genetics, Chinese Academy of Sciences, Datun Road, Beijing, Beijing 100101, P.R.China	Rat neural cell adhesion protein BIG-2 precursor, gi :1016012 Yoshihara, Y., Kawasaki, M., Tamada, A., Nagata, S., Kagamiyama, H. and Mori, K. J. Neurobiol. 28 (1), 51-69 (1995)	Membrane- bound
sbg29716 9-BGP	Biliary glycoprotein (BGP)	JGI: CITB- E1_2616J11 Submitted by Joint Genome Institute, Department of Energy, USA	Mouse biliary glycoprotein (BGP), gi:312584 McCuaig K, Rosenberg M, Nedellec P, Turbide C, and Beauchemin N; 1993; Gene 127:173- 83.	Secreted
sbg25391 9- HSCCAa	Human squamous cell carcinoma antigen (SCCA)	GB:AC019355 Submitted (02-JAN-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human squamous cell carcinoma antigen 2 (SCCA-2) (LEUPIN). gi:1710877. Schneider, S.S., Schick, C., Fish, K.E., Miller, E., Pena, J.C., Treter, S.D., Hui, S.M. and Silverman, G.A. Proc. Natl. Acad. Sci. U.S.A. 92 (8), 3147- 3151 (1995).	Secreted
sbg22813 7-OLF	Olfactomedin -related protein	GB:AC022606 Submitted (06- FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Rat neuronal olfactomedin-related protein precursor, gi:3024210 Danielson, P.E., Forss- Petter, S., Battenberg, E.L., deLecea, L., Bloom, F.E., and Sutcliffe, J.G., 1994, J. Neurosci. Res. 38:468- 478.	Secreted



Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg378514- Netrin	Netrin precursor	SC:BA5N16 Submitted (09-APR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Mouse Netrin-G1a protein gi:9909148 Nakashiba,T., Ikeda,T., Nishimura,S., Tashiro,K., Honjo,T., Culotti,J.G. and Itohara,S. J. Neurosci. 20 (17), 6540-6550 (2000)	Secreted
sbg253227. mucous matrix glycoprotein	Extracellular mucous matrix glycoprotein (EMMG)	GB:AC011647 Submitted (08-OCT-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human colon specific protein, geneseq:Y54368 Submitted by DIADEXUS LLC Publication number and date: WO9960161-A1, 25-NOV-99	Secreted
sbg262831- SIAa	Sialoadhesin	JGI:CITB- E1_3073N11 Found at Joint Genome Institute	Human sialic acid binding immunoglobulin-like lectin 8 long splice variant, gi: 9837433 Foussias,G., Yousef,G.M. and Diamandis,E.P. Biochem. Biophys. Res. Commun. 278 (3), 775- 781 (2000)	Secreted
sbg233728- LIPASE	Pancreatic lipase	GB:AC011098 Submitted (01-OCT-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Human pancreatic lipase precursor, gi:126318 Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8.	Secreted
sbg400455. -CRF	C1q-related factor (CRF)	GB:AC024339 Submitted (28-FEB-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Mouse Gliacolin, gi:10566471 Koide,T., Aso,A., Yorihuzi,T. and Nagata,K. J. Biol. Chem. 275 (36), 27957- 27963 (2000)	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg400612-KINASEa	Protein kinase	GB:AP001615 Submitted (04-APR-2000) to the DDBJ/EMBL/GenBank databases. Nobuyoshi Shimizu, Keio University, School of Medicine, Molecular Biology; 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan	Murine protein kinase/ankyrin homologue, gene seq: Y76079 Submitted by GENESIS RES & DEV CORP LTD Publication number and date: WO9955865-A1 04-NOV-99	Secreted
sbg381373-ACRP	Adipocyte complement-related protein (ACRP30)	JGI:RPCI-11_161M6 Found at Joint Genome Institute, Department of Energy, USA	Human adipocyte Complement-Related Protein (ACRP30R2), gene seq: Y44487. Submitted by SMITHKLINE BEECHAM CORP Publication number and date: WO9964629-A1, 16-DEC-99	Secreted
sbg401294-MEX-3	MEX-3(IAP)	GB:AC026956 Submitted (25-MAR-2000) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Caenorhabditis elegans MEX-3, gi:1644450 Draper,B.W., Mello,C.C., Bowerman,B., Hardin,J. and Priess,J.R. Cell 87 (2), 205-216 (1996)	Cytosolic (RNA-binding protein)
sbg247722-Cadherin	OB-Cadherin	GB:AL132780 Submitted (02-NOV-1999) by Genoscope - Centre National de Sequencage : BP 191 91006 EVRY cedex - FRANCE	Human OB-cadherin-1, gi:1377894 Okazaki,M., Takeshita,S., Kawai,S., Kikuno,R., Tsujimura,A., Kudo,A. and Amann,E. J. Biol. Chem. 269 (16), 12092-12098 (1994)	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg391057-THIPa	Thyroid hormone induced protein	SC:AL158153, SC:AL392044 Submitted (22-MAR-2001) and (02-MAR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human TANGO 239, geneseqp:B01432 Submitted by MILLENNIUM PHARM INC Publication number and date: WO200039284-A1, 06-JUL-00	Secreted
sbg378067-TGFc	TGF beta (transforming growth factor beta)	SC:AL162502 Submitted (06-APR-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human persephin growth factor, geneseqp:Y16714 Submitted by UNIV WASHINGTON Publication number and date: WO9914235-A1 25-MAR-99	Secreted

Table III.

Gene Name	Uses	Associated Diseases
sbg318680-DNase	An embodiment of the invention is the use of sbg318680-DNase to treat respiratory diseases and target parasites or cancer cells as a chromosome degrading agent to cause death of those cells. Close homologues of sbg318680-DNase are DNases. DNase can be used to treat respiratory diseases, such as pneumonia, cystic fibrosis and asthma, by reducing viscosity of bronchopulmonary secretions (MacConnachie AM; 1999; Intensive Crit Care Nurs 14:101-2).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation and respiratory diseases
sbg237038-SA	An embodiment of the invention is the use of sbg237038SA in blood pressure control. A close homologue of sbg237038SA is the rat SA gene. The SA gene is expressed at higher levels in the kidney of genetically hypertensive rats (Yang T, Hassan SA, Singh I, Smart A, Brosius FC, Holzman LB, Schnermann JB, Briggs JP; 1996; Hypertension 27:541-51).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and hypertension
sbg340871-GPV	An embodiment of the invention is the use of sbg340871-GPV in hemostasis and platelet aggregation. A close homologue of sbg340871-GPV is platelet glycoprotein (GP) V. Platelet glycoprotein (GP) V is a major surface protein which is cleaved by thrombin during platelet activation, and associates with GPIb-IX complex to form GPIb-V-IX, a receptor for von Willebrand factor and thrombin. Its functional role in hemostasis is possibly related to thrombin-induced platelet aggregation (Ravanat C, Morales M, Azorsa DO, Moog S, Schuhler S, Grunert P, Loew D, Van Dorsselaer A, Cazenave JP, Lanza F; 1997; Blood 89:3253-62).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and Bernard-Soulier disease
sbg293416-HNKS	An embodiment of the invention is the use of sbg293416-HNKS in cell interactions and the development of the nervous system. Close homologues of sbg293416-HNKS are sulfotransferases. Sulfotransferases are considered to be key enzymes in the biosynthesis of the HNK-1 carbohydrate epitope, which is expressed on several neural adhesion glycoproteins and as a glycolipid, and is involved in cell interactions (Bakker,H., Friedmann,I., Oka,S., Kawasaki,T., Nifant'ev,N., Schachner,M. and Mantei,N., 1997, J. Biol. Chem. 272:29942-29946). The HNK-1 epitope is spatially and temporally regulated during the development of the nervous system. The biological function of the HNK-1 sulfotransferase may be related to the development of the nervous system, and also may be involved in the preferential reinnervation of muscle nerves by motor axons after lesion (Jungalwala FB, 1994, Neurochem Res 19:945-57).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and peripheral neuropathies

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg257418-ZP	An embodiment of the invention is the use of sbg257418ZP in fertilization. A close homologue of sbg257418ZP is zona pellucida. Zona pellucida protein is an extracellular matrix that surrounds growing oocytes, ovulated eggs, and early embryos and it is critically involved in fertilization (Epifano, O., Liang, L.F., Familiar, M., Moos, M.C. Jr. and Dean, J.; 1995; Development 121:1947-1956). The zona pellucida also provides a post-fertilization block to polyspermy and protects the growing embryo as it passes down the oviduct (Rankin T, and Dean J; 1996; Mol Hum Reprod 2:889-94).	Infertility
sbg319185-CDa	An embodiment of the invention is the use of sbg319185CDa, a secreted protein, in the diagnosis and treatment of cancer and autoimmune disorders. Close homologues of sbg319185CDa are leukocyte differentiation antigen CD84 isoforms. CD84's are members of the immunoglobulin superfamily, show high homology with several molecules belonging to the CD2 family of differentiation antigens and is proposed to be useful in the diagnosis and treatment of cancer and autoimmune disorders (Palou E, Piroto F, Sole J, Freed JH, Peral B, Vilardell C, Vilella R, Vives J, Gaya A. Genomic characterization of CD84 reveals the existence of five isoforms differing in their cytoplasmic domains. Tissue Antigens 2000 Feb;55(2):118-27)).	Cancer, autoimmune disorders, wound healing disorders, infections and hematopoietic disorders
sbg323307-KIAAa	An embodiment of the invention is the use of sbg323307-KIAAa, a secreted protein, to regulate cell signaling, motility, and nucleic acid management. A close homologue of sbg323307-KIAAa is human KIAA0918 protein. Human KIAA0918 protein, a slit-like protein is functionally related to cell signaling/communication, cell structure/motility and nucleic acid management (Nagase, T., Ishikawa, K., Suyama, M., Kikuno, R., Hirose, M., Miyajima, N., Tanaka, A., Kotani, H., Nomura, N. and Ohara, O. KIAA0918 protein [Homo sapiens], DNA Res. 5 (6), 355-364 (1998)).	Cancer, autoimmune disorders, infections, wound healing disorders and hematopoietic disorders

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg315953-GPPa	An embodiment of the invention is the use of sbg315953GPPa, a secreted protein, to treat disorders associated with lipopolysaccharides. A close homologue to sbg315953GPPa is Bovine granulocyte peptide A precursor. Bovine granulocyte peptide A precursors are used in human and veterinary medicine, particularly to treat disorders associated with lipopolysaccharides, e.g. sepsis and endotoxaemia (1. Selsted ME, Bovine granulocyte peptide A precursor (antimicrobial BGP-A). Accession Number W23722, Publication Date 21-AUG-97. 2. Yount NY, Yuan J, Tarver A, Castro T, Diamond G, Tran PA, Levy JN, McCullough C, Cullor JS, Bevins CL, Selsted ME. Cloning and expression of bovine neutrophil beta-defensins. Biosynthetic profile during neutrophilic maturation and localization of mature peptide to novel cytoplasmic dense granules. J Biol Chem 1999 Sep 10;274(37):26249-58)).	Infections, cancer, autoimmune disorders, wounder healing disorders and hematopoietic disorders.
sbg318486-ONC	An embodiment of the invention is the use of sbg318486ONC in the growth and invasion events of trophoblast and tumor cells. A close homologue to sbg318486ONC is oncotrophoblast glycoproteins. It has been shown that oncotrophoblast protein was expressed by tumor cells with metastatic spread, suggesting a role in invasion during cancer (King,K.W., Sheppard,F.C., Westwater,C., Stern,P.L. and Myers,K.A.; 1999; Biochim. Biophys. Acta 1445, 257-270).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation
sbg299359-LIPO	An embodiment of the invention is the use of sbg299359LIPO in sperm maturation, taste recognition, and transportation of some molecules across the blood brain barrier. A close homologue to sbg299359LIPO is Lipocalin. Lipocalins transport small hydrophobic molecules such as steroids, bilins, retinoids, and lipids, and they have various effects on a number of tissues. It has been shown that lipocalins are involved in sperm maturation, taste recognition, and transportation of some molecules across the blood brain barrier (Newcomer M.E.; 1993; Structure 1:7-18; Achen M.G., Harms P.J., Thomas T., Richardson S.J., Wettenhall R.E.H., Schreiber G.; 1992; J. Biol. Chem. 267:23170-23174)	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg230022-NGa	An embodiment of the invention is the use of sbg230022Nga in the formation and maintenance of neuron type-specific networks in the brain. Close homologues to sbg230022Nga are mouse plasmacytoma-associated neuronal glycoprotein and rat BIG-1 protein. Mouse plasmacytoma-associated neuronal glycoprotein, is ectopically activated by intracisternal A-type particle long terminal repeats in murine plasmacytomas. Rat BIG-1 protein, is a TAG-1/F3-related member of the immunoglobulin superfamily with neurite outgrowth-promoting activity and involved in the formation and maintenance of neuron type-specific networks in the brain (1. Connelly MA, Grady RC, Mushinski JF, Marcu KB. PANG, a gene encoding a neuronal glycoprotein, is ectopically activated by intracisternal A-type particle long terminal repeats in murine plasmacytomas. Proc Natl Acad Sci U S A 1994 Feb 15;91(4):1337-41 2. Yoshihara Y, Kawasaki M, Tani A, Tamada A, Nagata S, Kagamiyama H, Mori K. BIG-1: a new TAG-1/F3-related member of the immunoglobulin superfamily with neurite outgrowth-promoting activity. Neuron 1994 Aug;13(2):415-26).	Cancer, infections, autoimmune disorders, wound healing disorders and hematopoietic disorders
sbg297169-BGP	An embodiment of the invention is the use of sbg297169BGP in renewal and/or differentiation of epithelial cells. A close homologue to sbg297169BGP is BGP protein. BGP proteins are expressed at the cell surface and function <i>in vitro</i> as cell adhesion molecules. The expression of the many BGP isoforms at the surface of epithelial cells, such as the colon, suggests that these proteins play a major role in renewal and/or differentiation of their epithelia (McCuaig K, Rosenberg M, Nedellec P, Turbide C, and Beauchemin N; 1993; Gene 127:173-83).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg253919-HSCCAa	<p>An embodiment of the invention is the use of sbg253919-HSCCAa for treatment of cancer or psoriasis or in development of more aggressive squamous cell carcinomas. Close homologues of sbg253919-HSCCAa are Psoriastatin type II and a human leupin precursor. Psoriastatin type II, is claimed to modulate activity of psoriastatin type I and II genes, e.g. using (ant)agonists, useful for treatment of cancer or psoriasis. The other, a human leupin precursor, contains a tandem duplication of the human squamous cell carcinoma antigen gene playing a causal role in development of more aggressive squamous cell carcinomas (1. Goetinck PF, Hibino T, Takahashi T and Baciu PC. Modulating cell proliferation or apoptosis - by modulating activity of psoriastatin type I and II genes, e.g. using (ant) agonists, useful for treatment of cancer or psoriasis. Accession Number W15242, publication date 24-APR-97. 2. Schneider SS, Schick C, Fish KE, Miller E, Pena JC, Treter SD, Hui SM, Silverman GA. A serine proteinase inhibitor locus at 18q21.3 contains a tandem duplication of the human squamous cell carcinoma antigen gene. Proc Natl Acad Sci U S A 1995 Apr 11;92(8):3147-51. 3. Barnes RC, Worrall DM. Identification of a novel human serpin gene; cloning sequencing and expression of leupin. FEBS Lett 1995 Oct 2; 373 (1): 61-5).</p>	Cancers, such as squamous cell carcinomas
sbg228137-OLF	<p>An embodiment of the invention is the use of sbg228137OLF in functional roles in chemoreception and in the central nervous system. A close homologue to sbg228137OLF is olfactomedin. Olfactomedin is a glycoprotein, and reacts with proteins of olfactory cilia. It was originally discovered at the mucociliary surface of the amphibian olfactory neuroepithelium and subsequently found throughout the mammalian brain (Danielson,P.E., Forss-Petter,S., Battenberg,E.L., deLecea,L., Bloom,F.E., and Sutcliffe,J.G., 1994, J. Neurosci. Res. 38:468-478). Its noticeable deposition at the chemosensory surface of the olfactory neuroepithelium suggest a role for this protein in chemoreception (Snyder DA, Rivers AM, Yokoe H, Menco BP, and Anholt RR, 1991, Biochemistry 30:9143-53). The widespread occurrence of olfactomedin among mammals in the brains also suggests its new functions in the central nervous system (Karavanich CA, and Anholt RR, 1998, Mol Biol Evol 15:718-26).</p>	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and nervous system disorders



Table III (cont).

Gene Name	Uses	Associated Diseases
sbg378514-Netrin	An embodiment of the invention is the use of sbg378514-Netrin in roles of the central nervous system. A close homologue to sbg378514-Netrin is Netrin. Netrins possess commissural axon outgrowth-promoting activity, and control guidance of CNS commissural axons and peripheral motor axons (Serafini T, Kennedy TE, Galko MJ, Mirzayan C, Jessell TM, and Tessier-Lavigne M; 1994; Cell 78:409-24). Diffusible and substrate-bound cues, including netrins and their receptors, can guide axonal pathway choice via attractive and repulsive signals (Tear G; 1998; Essays Biochem 33:1-13).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and nervous system disorder
sbg253227.mucous matrix glycoprotein	An embodiment of the invention is the use of sbg253227.-mucous matrix glycoprotein for the treatment of gastrointestinal disorders and cancer. Close homologues of sbg253227.mucous matrix glycoprotein have been used in combination for treatment of infections associated with EMMG. EMMG is useful for the treatment of gastrointestinal disorders and cancer, e.g. dysphagia, abdominal angina, pancreatitis, colonic carcinoma, Crohn's disease and the Mallory-Weiss syndrome (US5929033-A, CORLEY NC, TANG YT, Submitted by INCYTE PHARM INC. Reference number, WPI; 99-429518/36, 1999).	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases Neurological disorders, gastrointestinal disorders, dysphagia, abdominal angina, pancreatitis, colonic carcinoma, Crohn's disease and the Mallory-Weiss syndrome.
sbg262831-SIAa	An embodiment of the invention is the use of sbg262831SIAa to mediate sialic acid-dependent ligand recognition and to function as an inhibitory receptor in human natural killer cells. A close homologue of sbg262831SIAa is human QA79 membrane protein. QA79 belongs to the sialoadhesin family and is proposed to mediate sialic acid-dependent ligand recognition and to function as an inhibitory receptor in human natural killer cells (Falco, M., Biassoni, R., Bottino, C., Vitale, M., Sivori, S., Augugliaro, R., Moretta, L. and Moretta, A. Identification and molecular cloning of p75/AIRM1, a novel member of the sialoadhesin family that functions as an inhibitory receptor in human natural killer cells. J Exp Med 1999 Sep 20;190(6):793-802).	Cancer, autoimmune disorders, infection, wound healing disorders, and hematopoietic disorders.

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg233728-LIPASE	An embodiment of the invention is the use of sbg233728LIPASE to treat pancreatitis via replacement therapy. A close homologue of sbg233728-LIPASE is pancreatic lipase. Pancreatic lipase can be used as replacement enzymes for patients with chronic pancreatitis. Pancreatic lipase hydrolyzes dietary long chain triacylglycerol to free fatty acids and monoacylglycerols in the intestinal lumen (Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8). Pancreatic steatorrhea and pancreatic diabetes are the dominant symptoms of patients in a certain stage of chronic pancreatitis. In this stage, the nutritional state is greatly disturbed and hypoglycemia and labile infection are involved. Pancreatic enzyme replacement therapy is the principal treatment method for pancreatic steatorrhea. (Nakamura T, Takeuchi T, and Tando Y; 1998; Pancreas 16:329-36).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, and pancreatitis.
sbg400455.-CRF	An embodiment of the invention is the use of sbg400455.CRF in the areas of the nervous system involved in motor function, such as the Purkinje cells of the cerebellum, the accessory olivary nucleus, the pons, and the red nucleus. Close homologues of sbg400455.CRF include CRF transcripts. CRF transcripts are most abundant in areas of the nervous system and have been used to develop products for modulating energy balance or insulin production in mammals ((W09639429-A2) Schere, P.E.; Submitted by Whithead Institute of Biomedical Research; Berube NG, Swanson XH, Bertram MJ, Kittle JD, Didenko V, Baskin DS, Smith JR and Pereira-Smith OM., Brain Res. Mol. Brain Res. 63 (2), 233-240 (1999)).	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases, energy homeostasis disorder and obesity
sbg400612-KINASEa	An embodiment of the invention is the use of sbg400612-KINASEa in the treatment of inflammation, cancer, neurological diseases, growth and developmental defects, skin wounds, and hair follicle disorders. A close homologue of sbg400612-KINASEa is murine protein kinase/ ankyrin homologue. Murine protein kinase/ ankyrin homologue can stimulate the growth and motility of keratinocytes, inhibit the growth of cancer cells, modulate angiogenesis and tumour vascularisation, modulate skin inflammation and epithelial cell growth and inhibit binding of HIV-1 to leukocytes. Murine protein kinase/ ankyrin homologue can also be used to treat inflammation, cancer, neurological diseases, growth and developmental defects, skin wounds, and hair follicle disorders (Kumble A, Murison JG, Onrust R, Sleeman M, Strachan L and Watson JD. Novel polynucleotides useful for the treatment of various conditions including wounds and cancer. Accession Number: Y76079 Publication Date: 04-NOV-99).	Cancer, wound healing disorders, autoimmune disorders, hematopoietic disorders and infection

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg381373-ACRP	An embodiment of the invention is the use of sbg381373-ACRP in the complex balanced system of energy homeostasis involving food intake, carbohydrate catabolism, and lipid catabolism. A close homologue of sbg381373-ACRP is ACRP30 protein. ACRP30 protein may be a factor that participates in the complex balanced system of energy homeostasis involving food intake, carbohydrate catabolism, and lipid catabolism. ACRP30 is structurally similar to complement factor C1q, and it forms large homo-oligomers that undergo a series of post-translational modifications (Scherer PE, Williams S, Fogliano M, Baldini G, Lodish HF; 1995; J Biol Chem 270:26746-9).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, obesity, and diabetes
sbg401294-MEX-3	An embodiment of the invention is the use of sbg401294-MEX-3 to develop products for diagnosis and therapy of disease states such as tumor formation, apoptosis regulation in cells to reduce or increase apoptosis and for pharmacological screening.	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, tumor formation, autoimmune diseases, inhibition of apoptosis
sbg247722-Cadherin	An embodiment of the invention is the use of sbg247722-Cadherin for treatment and diagnosis of bone metabolic diseases. A close homologue of sbg247722-Cadherin is cadherin, a Ca <sup>2+</sup> dependent cell adhesion protein.	Hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, autoimmune diseases, energy homeostasis disorder and bone metabolic disease
sbg391057-THIPa	An embodiment of the invention is the use of sbg391057-THIPa in controlling thyroid hormone synthesis. A close homologue of sbg391057-THIPa is xenopus laevis thyroid hormone-induced protein. Xenopus laevis thyroid hormone-induced protein has been implicated in controlling thyroid hormone synthesis in Xenopus tadpoles and provided insights into the biology of metamorphosis (Brown,D.D., Wang,Z., Furlow,J.D., Kanamori,A., Schwartzman, R.A., Remo,B.F. and Pinder,A. The thyroid hormone-induced tail resorption program during Xenopus laevis metamorphosis. Proc Natl Acad Sci U S A 1996 Mar 5;93(5):1924-9).	Autoimmune disorders, wound healing disorders, cancer, infection and hematopoietic disorders

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg378067-TGFc	<p>An embodiment of the invention is the use of sbg378067-TGFc in cellular growth control in the etiology of cancer and cell differentiation and development. The sbg378067-TGFc protein contains a close approximation of the prosite consensus pattern (PDOC00223) for TGF-beta family members. TGF-beta proteins have been known to be involved in growth control and hence the etiology of cancer (<i>Anticancer Res</i> 1999 Nov-Dec;19(6A):4791-807), cell differentiation and development. A TGF-beta signaling pathway constitutes a tumor suppressor path (<i>Cytokine Growth Factor Rev</i> 2000 Apr 1;11(1-2):159-168). A close homologue of sbg378067-TGFc is TGF-beta protein.</p>	<p>Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, preventing or treating cellular degeneration or insufficiency, e.g. neuronal degeneration resulting from peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, ischemic stroke, acute brain injury, acute spinal cord injury, nervous system tumours, multiple sclerosis, or infection (viral, bacterial, fungal, parasitic), hematopoietic cell degeneration or insufficiency resulting from eosinopenia, anemias, thrombocytopenia, or stem-cell insufficiencies, cardiac muscle degeneration or insufficiency resulting from cardiomyopathy or congestive heart failure, peripheral nerve trauma or injury, exposure to neurotoxins, metabolic diseases such as diabetes or renal dysfunctions and damage caused by infectious agents</p>

**Table IV. Quantitative, Tissue-specific mRNA expression detected using SybrMan**

Quantitative, tissue-specific, mRNA expression patterns of the genes were measured using SYBR-Green Quantitative PCR (Applied Biosystems, Foster City, CA; see Schmittgen T.D. et al., Analytical Biochemistry 285:194-204, 2000) and human cDNAs prepared from various human tissues. Gene-specific PCR primers were designed using the first nucleic acid sequence listed in the Sequence List for each gene. Results are presented as the number of copies of each specific gene's mRNA detected in 1ng mRNA pool from each tissue. Two replicate mRNA measurements were made from each tissue RNA.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)									
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine	Spleen/lymph	Placenta	Testis
sbg237038SA	14 $\pm$ 1	27 $\pm$ 1	39 $\pm$ 1	14 $\pm$ 0	18 $\pm$ 1	12 $\pm$ 0	21 $\pm$ 3	45 $\pm$ 2	19 $\pm$ 3	40 $\pm$ 9
sbg340871-GPV	0 $\pm$ 0	200 $\pm$ 46	363 $\pm$ 10	-9 $\pm$ 6	33 $\pm$ 13	93 $\pm$ 17	74 $\pm$ 9	305 $\pm$ 9	2902 $\pm$ 114	36 $\pm$ 4
sbg293416-HNKS	553 $\pm$ 15	65 $\pm$ 1	39 $\pm$ 4	27 $\pm$ 4	39 $\pm$ 1	38 $\pm$ 1	53 $\pm$ 4	225 $\pm$ 9	43 $\pm$ 0	108 $\pm$ 9
sbg257418ZP	37 $\pm$ 3	28 $\pm$ 6	6 $\pm$ 0	-12 $\pm$ 3	-4 $\pm$ 2	19 $\pm$ 7	15 $\pm$ 2	5 $\pm$ 2	10 $\pm$ 2	605 $\pm$ 10
sbg319185-CDa	54 $\pm$ 5	113 $\pm$ 3	696 $\pm$ 140	95 $\pm$ 37	317 $\pm$ 31	708 $\pm$ 30	540 $\pm$ 64	5987 $\pm$ 158	326 $\pm$ 2	258 $\pm$ 31
sbg323307-KIAAa	293 $\pm$ 8	633 $\pm$ 15	1269 $\pm$ 58	15 $\pm$ 1	136 $\pm$ 5	26 $\pm$ 6	1400 $\pm$ 91	33 $\pm$ 12	632 $\pm$ 12	196 $\pm$ 10
sbg315953-GPPa	232 $\pm$ 31	16 $\pm$ 0	54 $\pm$ 2	1 $\pm$ 6	14 $\pm$ 7	4 $\pm$ 8	15 $\pm$ 3	99 $\pm$ 4	61 $\pm$ 7	126 $\pm$ 6
sbg318486-ONC	52 $\pm$ 7	3 $\pm$ 2	8 $\pm$ 0	4 $\pm$ 0	4 $\pm$ 2	2 $\pm$ 1	6 $\pm$ 2	1 $\pm$ 7	4 $\pm$ 1	122 $\pm$ 9
sbg299359-LIPO	1701 $\pm$ 95	39 $\pm$ 0	60 $\pm$ 14	21 $\pm$ 1	135 $\pm$ 13	41 $\pm$ 3	49 $\pm$ 2	26 $\pm$ 7	40 $\pm$ 5	138 $\pm$ 2

Table IV (cont.)

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)									
	Brain	Heart	Lung	Liver	Kid- ney	Skele- tal muscle	Intes- tine	Spleen /lymph	Pla- centa	Testis
sbg230022- NGa	3443 $\pm$ 112	684 $\pm$ 2	386 $\pm$ 7	712 $\pm$ 16	1956 $\pm$ 63	36 $\pm$ 0	588 $\pm$ 7	1293 $\pm$ 17	43 $\pm$ 7	358 $\pm$ 2
sbg297169- BGP	417 $\pm$ 29	141 $\pm$ 8	236 $\pm$ 5	170 $\pm$ 11	322 $\pm$ 0	74 $\pm$ 4	231 $\pm$ 1	370 $\pm$ 0	223 $\pm$ 3	968 $\pm$ 32
sbg253919- HSCCAa	-5 $\pm$ 1	1 $\pm$ 1	2 $\pm$ 1	-14 $\pm$ 2	-10 $\pm$ 0	-4 $\pm$ 3	0 $\pm$ 1	6 $\pm$ 1	4 $\pm$ 3	119 $\pm$ 9
sbg228137- OLF	5174 $\pm$ 138	58 $\pm$ 4	99 $\pm$ 5	9 $\pm$ 3	63 $\pm$ 7	167 $\pm$ 12	98 $\pm$ 0	719 $\pm$ 9	32 $\pm$ 8	67 $\pm$ 4
sbg253227. mucous matrix glycoprotein	5 $\pm$ 0	11 $\pm$ 1	21 $\pm$ 1	0 $\pm$ 1	28 $\pm$ 2	1 $\pm$ 0	13 $\pm$ 2	24 $\pm$ 3	26 $\pm$ 4	118 $\pm$ 1
sbg262831- SIAa	9 $\pm$ 1	6 $\pm$ 1	59 $\pm$ 1	59 $\pm$ 1	5 $\pm$ 0	-4 $\pm$ 2	134 $\pm$ 6	2657 $\pm$ 97	45 $\pm$ 4	25 $\pm$ 0
sbg233728- LIPASE	2 $\pm$ 1	6 $\pm$ 1	4 $\pm$ 2	6 $\pm$ 2	1 $\pm$ 0	4 $\pm$ 0	1 $\pm$ 3	1 $\pm$ 2	3 $\pm$ 2	28 $\pm$ 3
sbg400455.- CRF	8735 $\pm$ 257	345 $\pm$ 14	434 $\pm$ 54	191 $\pm$ 14	4038 $\pm$ 147	705 $\pm$ 32	379 $\pm$ 1	847 $\pm$ 59	434 $\pm$ 8	97 $\pm$ 8
sbg400612- KINASEa	10 $\pm$ 0	24 $\pm$ 4	276 $\pm$ 87	145 $\pm$ 2	431 $\pm$ 10	7 $\pm$ 0	59 $\pm$ 5	23 $\pm$ 4	82 $\pm$ 9	34 $\pm$ 3
sbg381373- ACRP	112 $\pm$ 40	11 $\pm$ 3	15 $\pm$ 5	14 $\pm$ 5	10 $\pm$ 2	11 $\pm$ 8	14 $\pm$ 4	-3 $\pm$ 8	6 $\pm$ 2	11 $\pm$ 8
sbg401294- MEX-3	49 $\pm$ 8	39 $\pm$ 2	122 $\pm$ 1	35 $\pm$ 9	151 $\pm$ 8	6 $\pm$ 5	16 $\pm$ 1	15 $\pm$ 3	71 $\pm$ 8	683 $\pm$ 56
sbg247722- Cadherin	2626 $\pm$ 18	1140 $\pm$ 22	1733 $\pm$ 62	78 $\pm$ 4	2007 $\pm$ 12	213 $\pm$ 52	1175 $\pm$ 47	1701 $\pm$ 167	3487 $\pm$ 263	1814 $\pm$ 30
sbg391057- THIPa	332 $\pm$ 3	3010 $\pm$ 30	8567 $\pm$ 84	136 $\pm$ 1	1013 $\pm$ 90	1499 $\pm$ 172	2469 $\pm$ 86	3512 $\pm$ 23	1393 $\pm$ 32	2408 $\pm$ 174
sbg378067- TGFC	33 $\pm$ 8	58 $\pm$ 6	52 $\pm$ 4	3 $\pm$ 1	48 $\pm$ 1	49 $\pm$ 22	21 $\pm$ 4	116 $\pm$ 28	74 $\pm$ 2 4	59 $\pm$ 4

Table V. Additional diseases based on mRNA expression in specific tissues

Tissue Expression	Additional Diseases
Brain	Neurological and psychiatric diseases, including Alzheimers, parasupranuclear palsey, Huntington's disease, myotonic dystrophy, anorexia, depression, schizophrenia, headache, amnesias, anxiety disorders, sleep disorders, multiple sclerosis
Heart	Cardiovascular diseases, including congestive heart failure, dilated cardiomyopathy, cardiac arrhythmias, Hodgson's Disease, myocardial infarction, cardiac arrhythmias
Lung	Respiratory diseases, including asthma, Chronic Obstructive Pulmonary Disease, cystic fibrosis, acute bronchitis, adult respiratory distress syndrome
Liver	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, cirrhosis, hepatic encephalopathy, fatty hepatocirrhosis, viral and nonviral hepatitis, Type II Diabetes Mellitis, impaired glucose tolerance
Kidney	Renal diseases, including acute and chronic renal failure, acute tubular necrosis, cystinuria, Fanconi's Syndrome, glomerulonephritis, renal cell carcinoma, renovascular hypertension
Skeletal muscle	Eulenburg's Disease, hypoglycemia, obesity, tendinitis, periodic paralyses, malignant hyperthermia, paramyotonia congenita, myotonia congenita
Intestine	Gastrointestinal diseases, including Myotonia congenita, Ileus, Intestinal Obstruction, Tropical Sprue, Pseudomembranous Enterocolitis
Spleen/lymph	Lymphangiectasia, hypersplenism, angiomas, ankylosing spondylitis, Hodgkin's Disease, macroglobulinemia, malignant lymphomas, rheumatoid arthritis
Placenta	Choriocarcinoma, hydatidiform mole, placenta previa
Testis	Testicular cancer, male reproductive diseases, including low testosterone and male infertility
Pancreas	Diabetic ketoacidosis, Type 1 & 2 diabetes, obesity, impaired glucose tolerance

**What is claimed is:**

1. An isolated polypeptide selected from the group consisting of:
  - (a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in  
5 Table I;
  - (b) an isolated polypeptide comprising a polypeptide sequence set forth in Table I; and
  - (c) a polypeptide sequence of a gene set forth in Table I.
2. An isolated polynucleotide selected from the group consisting of:
  - 10 (a) an isolated polynucleotide comprising a polynucleotide sequence set forth in Table I;
  - (b) an isolated polynucleotide of a gene set forth in Table I;
  - (c) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide  
set forth in Table I;
  - (d) an isolated polynucleotide encoding a polypeptide set forth in Table I;
  - 15 (e) a polynucleotide which is an RNA equivalent of the polynucleotide of (a) to (d);  
or a polynucleotide sequence complementary to said isolated polynucleotide.
3. An expression vector comprising a polynucleotide capable of producing a polypeptide of  
claim 1 when said expression vector is present in a compatible host cell.  
20
4. A process for producing a recombinant host cell which comprises the step of introducing  
an expression vector comprising a polynucleotide capable of producing a polypeptide of claim  
1 into a cell such that the host cell, under appropriate culture conditions, produces said  
polypeptide.  
25
5. A recombinant host cell produced by the process of claim 4.
6. A membrane of a recombinant host cell of claim 5 expressing said polypeptide.
- 30 7. A process for producing a polypeptide which comprises culturing a host cell of claim 5  
under conditions sufficient for the production of said polypeptide and recovering said  
polypeptide from the culture.



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&lt;210&gt; 22

&lt;211&gt; 1458

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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&lt;210&gt; 23

&lt;211&gt; 861

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

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&lt;210&gt; 24

&lt;211&gt; 1602

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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&lt;210&gt; 25

&lt;211&gt; 1488

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 25

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&lt;211&gt; 1053

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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&lt;210&gt; 27

&lt;211&gt; 1860

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

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&lt;210&gt; 28

&lt;211&gt; 1473

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

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&lt;211&gt; 1389

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 29

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&lt;210&gt; 30

&lt;211&gt; 768

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

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&lt;210&gt; 31

&lt;211&gt; 2355

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 31

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&lt;210&gt; 32

&lt;211&gt; 759

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 32

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&lt;210&gt; 33

&lt;211&gt; 1782

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 33

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&lt;210&gt; 34

&lt;211&gt; 1419

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 34

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&lt;210&gt; 35

&lt;211&gt; 1824

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 35

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&lt;210&gt; 36

&lt;211&gt; 2346

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 36

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&lt;210&gt; 37

&lt;211&gt; 1923

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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taa						1923

<210> 38  
 <211> 2061  
 <212> DNA  
 <213> Homo sapiens

<400> 38

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gaagccattc	gaggagtatc	aataagaagt	gatattgcca	ttgatgatgt	taaatttcag	1980
gcaggaccct	gtggagaaat	ggaagataca	actcaacaat	catcaggata	ttctgaggac	2040
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<210> 39  
 <211> 465  
 <212> DNA  
 <213> Homo sapiens

<400> 39

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catggccagg	atatatttcc	agcagagaag	ctctgtcatc	tgaggatttg	caagggtgaa	180
cttcacagag	ctgcctgcgg	tgagtgtatt	gttgaccca	agacttccag	cttcccttac	240
tgtcagggga	cctgcctgac	cctcaacagt	gagcttcac	aatccaactt	tgcactcaaa	300
gtttgacta	taagagggga	gtgcctattg	atctgttcc	ggctctttca	gacctgtagt	360
cccaccaagg	tcattctctt	ctccctaacg	gtccaggatg	acgaacgtaa	gatgagcgtt	420

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465

<210> 40  
 <211> 277  
 <212> PRT  
 <213> Homo sapiens

<400> 40  
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 Thr Glu Ala Phe Arg Ile Cys Ala Phe Asn Ala His Arg Leu Thr Leu  
 20 25 30  
 Ala Lys Leu Thr Lys Glu Ser Val Met Asp Thr Leu Val Gln Ile Leu  
 35 40 45  
 Ala Arg Cys Asp Ile Met Val Leu Gln Glu Val Val Asp Ser Ser Gln  
 50 55 60  
 Asn Thr Val Pro Phe Leu Leu Gln Lys Leu Lys Ser Ser Arg Ser Tyr  
 65 70 75 80  
 Ser Phe Leu Asn Ser Ser Leu Leu Gly Arg Ser Thr Tyr Lys Glu Lys  
 85 90 95  
 Tyr Val Tyr Ile Tyr Arg Ser Asp Lys Thr Gln Val Leu Asn Phe Tyr  
 100 105 110  
 Gln Tyr Asn Asp Thr Asp Asp Ile Phe Ala Arg Glu Pro Phe Val Ala  
 115 120 125  
 His Phe Thr Leu Pro Ser Lys Thr Leu Pro Ser Val Val Leu Val Pro  
 130 135 140  
 Leu His Thr Thr Pro Lys Asp Val Glu Lys Glu Leu Asn Ala Leu Tyr  
 145 150 155 160  
 Asp Val Phe Leu Asp Val Tyr Gln Arg Trp Gln Asn Glu Asn Val Ile  
 165 170 175  
 Leu Leu Gly Asp Phe Asn Ala Asp Cys Ala Ser Leu Thr Lys Lys Arg  
 180 185 190  
 Leu Lys Ser Leu Leu Leu Arg Thr Lys Ala Gly Phe His Trp Val Ile  
 195 200 205  
 Pro Asp Gly Glu Asp Thr Thr Val Arg Ala Ser Thr Asn Cys Thr Tyr  
 210 215 220  
 Asp Arg Ile Val Val His Gly Gln Gly Cys Gln Met Leu Leu Lys Ala  
 225 230 235 240  
 Ala Ala Thr Phe Asp Phe Pro Lys Arg Phe Gln Leu Thr Glu Glu Glu  
 245 250 255  
 Ala Leu Arg Ile Ser Asp His Tyr Pro Val Glu Val Glu Leu Ser Gln  
 260 265 270  
 Ala Thr Pro Leu Ser  
 275

<210> 41  
 <211> 480  
 <212> PRT  
 <213> Homo sapiens

<400> 41  
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 Ile Arg Pro Pro Asp Ser Arg Cys Leu Val Gln Ala Val Ser Gln Asn  
 35 40 45  
 Phe Asn Phe Ala Lys Asp Val Leu Asp Gln Trp Ser Gln Leu Glu Lys  
 50 55 60

Asp	Gly	Leu	Arg	Gly	Pro	Tyr	Pro	Ala	Leu	Trp	Lys	Val	Ser	Ala	Lys
65					70					75					80
Gly	Glu	Glu	Asp	Lys	Trp	Ser	Phe	Glu	Arg	Met	Thr	Gln	Leu	Ser	Lys
				85					90						95
Lys	Ala	Ala	Ser	Ile	Leu	Ser	Asp	Thr	Cys	Ala	Leu	Ser	His	Gly	Asp
			100					105					110		
Arg	Leu	Met	Ile	Ile	Leu	Pro	Pro	Thr	Pro	Glu	Ala	Tyr	Trp	Ile	Cys
		115					120						125		
Leu	Ala	Cys	Val	Arg	Leu	Gly	Ile	Thr	Phe	Val	Pro	Gly	Ser	Pro	Gln
	130					135					140				
Leu	Thr	Ala	Lys	Lys	Ile	Arg	Tyr	Gln	Leu	Arg	Met	Ser	Lys	Ala	Gln
145					150					155					160
Cys	Ile	Val	Ala	Asn	Glu	Ala	Met	Ala	Pro	Val	Val	Asn	Ser	Ala	Val
				165					170					175	
Ser	Asp	Cys	Pro	Thr	Leu	Lys	Thr	Lys	Leu	Leu	Val	Ser	Asp	Lys	Ser
		180						185					190		
Tyr	Asp	Gly	Trp	Leu	Asp	Phe	Lys	Lys	Leu	Ile	Gln	Val	Ala	Pro	Pro
	195						200						205		
Lys	Gln	Thr	Tyr	Met	Arg	Thr	Lys	Ser	Gln	Asp	Pro	Met	Ala	Ile	Phe
	210					215					220				
Phe	Thr	Lys	Gly	Thr	Thr	Gly	Ala	Pro	Lys	Met	Val	Glu	Tyr	Ser	Gln
225					230					235					240
Tyr	Gly	Leu	Gly	Met	Gly	Phe	Ser	Gln	Ala	Ser	Arg	Arg	Trp	Met	Asp
				245					250					255	
Leu	Gln	Pro	Thr	Asp	Val	Leu	Trp	Ser	Leu	Gly	Asp	Ala	Phe	Gly	Gly
			260					265					270		
Ser	Leu	Ser	Leu	Ser	Ala	Val	Leu	Gly	Thr	Trp	Phe	Gln	Gly	Ala	Cys
	275						280					285			
Val	Phe	Leu	Cys	His	Met	Pro	Thr	Phe	Cys	Pro	Glu	Thr	Val	Leu	Asn
	290					295					300				
Val	Leu	Ser	Arg	Phe	Pro	Ile	Thr	Thr	Leu	Ser	Ala	Asn	Pro	Glu	Met
305					310					315					320
Tyr	Gln	Glu	Leu	Leu	Gln	His	Lys	Cys	Phe	Thr	Ser	Tyr	Arg	Phe	Lys
				325					330					335	
Ser	Leu	Lys	Gln	Cys	Val	Ala	Ala	Gly	Gly	Pro	Ile	Ser	Pro	Gly	Val
			340					345					350		
Ile	Glu	Asp	Trp	Lys	Arg	Ile	Thr	Lys	Leu	Asp	Ile	Tyr	Glu	Gly	Tyr
	355						360					365			
Gly	Gln	Thr	Glu	Thr	Gly	Leu	Leu	Cys	Ala	Thr	Ser	Lys	Thr	Ile	Lys
	370				375						380				
Leu	Lys	Pro	Ser	Ser	Leu	Gly	Lys	Pro	Leu	Pro	Pro	Tyr	Ile	Val	Gln
385					390					395					400
Ile	Val	Asp	Glu	Asn	Ser	Asn	Leu	Leu	Pro	Gly	Glu	Glu	Gly	Asn	
				405					410					415	
Ile	Ala	Ile	Arg	Ile	Lys	Leu	Asn	Gln	Pro	Ala	Ser	Leu	Tyr	Cys	Pro
			420					425					430		
His	Met	Val	Ser	Trp	Glu	Glu	Tyr	Ala	Ser	Ala	Arg	Gly	His	Met	Leu
	435						440					445			
Tyr	Leu	Thr	Gly	Asp	Arg	Gly	Ile	Met	Asp	Glu	Asp	Gly	Tyr	Phe	Trp
	450					455					460				
Trp	Ser	Gly	Arg	Val	Asp	Val	Ala	Asn	Ala	Leu	Gly	Gln	Arg	Leu	
465					470				475					480	

&lt;210&gt; 42

&lt;211&gt; 583

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42



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Met Leu Gly Arg Phe Gln Pro Phe Ser Leu Val Arg Ser Phe Arg Leu
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Gly Phe Gly Ala Cys Cys Tyr Pro Asn Gln Lys Cys Ala Thr Gln Thr
      20      25      30
Ile Arg Pro Pro Asp Ser Arg Cys Leu Val Gln Ala Val Ser Gln Asn
      35      40      45
Phe Asn Phe Ala Lys Asp Val Leu Asp Gln Trp Ser Gln Leu Glu Lys
      50      55      60
Asp Gly Leu Arg Gly Pro Tyr Pro Ala Leu Trp Lys Val Ser Ala Lys
65      70      75      80
Gly Glu Glu Asp Lys Trp Ser Phe Glu Arg Met Thr Gln Leu Ser Lys
      85      90      95
Lys Ala Ala Ser Ile Leu Ser Asp Thr Cys Ala Leu Ser His Gly Asp
      100      105      110
Arg Leu Met Ile Ile Leu Pro Pro Thr Pro Glu Ala Tyr Trp Ile Cys
      115      120      125
Leu Ala Cys Val Arg Leu Gly Ile Thr Phe Val Pro Gly Ser Pro Gln
      130      135      140
Leu Thr Ala Lys Lys Ile Arg Tyr Gln Leu Arg Met Ser Lys Ala Gln
145      150      155      160
Cys Ile Val Ala Asn Glu Ala Met Ala Pro Val Val Asn Ser Ala Val
      165      170      175
Ser Asp Cys Pro Thr Leu Lys Thr Lys Leu Leu Val Ser Asp Lys Ser
      180      185      190
Tyr Asp Gly Trp Leu Asp Phe Lys Lys Leu Ile Gln Val Ala Pro Pro
      195      200      205
Lys Gln Thr Tyr Met Arg Thr Lys Ser Gln Asp Pro Met Ala Ile Phe
      210      215      220
Phe Thr Lys Gly Thr Thr Gly Ala Pro Lys Met Val Glu Tyr Ser Gln
225      230      235      240
Tyr Gly Leu Gly Met Gly Phe Ser Gln Ala Ser Arg Arg Trp Met Asp
      245      250      255
Leu Gln Pro Thr Asp Val Leu Trp Ser Leu Gly Asp Ala Phe Gly Gly
      260      265      270
Ser Leu Ser Leu Ser Ala Val Leu Gly Thr Trp Phe Gln Gly Ala Cys
      275      280      285
Val Phe Leu Cys His Met Pro Thr Phe Cys Pro Glu Thr Val Leu Asn
      290      295      300
Val Leu Ser Arg Phe Pro Ile Thr Thr Leu Ser Ala Asn Pro Glu Met
305      310      315      320
Tyr Gln Glu Leu Leu Gln His Lys Cys Phe Thr Ser Tyr Arg Phe Lys
      325      330      335
Ser Leu Lys Gln Cys Val Ala Ala Gly Gly Pro Ile Ser Pro Gly Val
      340      345      350
Ile Glu Asp Trp Lys Arg Ile Thr Lys Leu Asp Ile Tyr Glu Gly Tyr
      355      360      365
Gly Gln Thr Glu Thr Gly Leu Leu Cys Ala Thr Ser Lys Thr Ile Lys
      370      375      380
Leu Lys Pro Ser Ser Leu Gly Lys Pro Leu Pro Pro Tyr Ile Val Gln
385      390      395      400
Ile Val Asp Glu Asn Ser Asn Leu Leu Pro Pro Gly Glu Glu Gly Asn
      405      410      415
Ile Ala Ile Arg Ile Lys Leu Asn Gln Pro Ala Ser Leu Tyr Cys Pro
      420      425      430
His Met Val Ser Trp Glu Glu Tyr Ala Ser Ala Arg Gly His Met Leu
      435      440      445
Tyr Leu Thr Gly Asp Arg Gly Ile Met Asp Glu Asp Gly Tyr Phe Trp
      450      455      460
Trp Ser Gly Arg Val Asp Asp Val Ala Asn Ala Leu Gly Gln Arg Phe

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465					470					475				480
Ser	Arg	Pro	Gly	Ala	Ala	Ala	Ala	Ala	Ser	Ala	Val	Gly	Ala	Pro
				485					490					495
Gly	Gly	Trp	His	Ser	Leu	Cys	Ala	Ser	Val	Pro	Ile	Leu	Gln	Val
			500					505					510	
Lys	Pro	Pro	Asn	Val	Leu	Thr	Pro	Gln	Phe	Leu	Ser	His	Asp	Gln
		515					520					525		Gly
Gln	Leu	Thr	Lys	Glu	Leu	Gln	Gln	His	Ile	Lys	Ser	Val	Thr	Gly
	530					535					540			Pro
Cys	Lys	Tyr	Gln	Arg	Lys	Val	Glu	Phe	Val	Pro	Glu	Leu	Pro	Lys
545					550					555				560
Val	Thr	Gly	Lys	Ile	Lys	Arg	Glu	Leu	Gln	Val	Trp	Ser	Asp	Val
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Ser	Ser	Glu	Leu	Arg	Asn	Asp								
			580											

<210> 43  
 <211> 581  
 <212> PRT  
 <213> Homo sapiens

<400> 43

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			20					25					30		
Arg	Ala	Ser	Gln	Val	Glu	Cys	Thr	Gly	Ala	Arg	Ile	Val	Ala	Val	Pro
		35					40					45			
Thr	Pro	Leu	Pro	Trp	Asn	Ala	Met	Ser	Leu	Gln	Ile	Leu	Asn	Thr	His
	50				55						60				
Ile	Thr	Glu	Leu	Asn	Glu	Ser	Pro	Phe	Leu	Asn	Ile	Ser	Ala	Leu	Ile
65				70						75				80	
Ala	Leu	Arg	Ile	Glu	Lys	Asn	Glu	Leu	Ser	Arg	Ile	Thr	Pro	Gly	Ala
			85						90					95	
Phe	Arg	Asn	Leu	Gly	Ser	Leu	Arg	Tyr	Leu	Ser	Leu	Ala	Asn	Asn	Lys
		100						105					110		
Leu	Gln	Val	Leu	Pro	Ile	Gly	Leu	Phe	Gln	Gly	Leu	Asp	Ser	Leu	Glu
	115						120					125			
Ser	Leu	Leu	Leu	Ser	Ser	Asn	Gln	Leu	Leu	Gln	Ile	Gln	Pro	Ala	His
	130					135					140				
Phe	Ser	Gln	Cys	Ser	Asn	Leu	Lys	Glu	Leu	Gln	Leu	His	Gly	Asn	His
145				150					155					160	
Leu	Glu	Tyr	Ile	Pro	Asp	Gly	Ala	Phe	Asp	His	Leu	Val	Gly	Leu	Thr
			165						170					175	
Lys	Leu	Asn	Leu	Gly	Lys	Asn	Ser	Leu	Thr	His	Ile	Ser	Pro	Arg	Val
		180						185					190		
Phe	Gln	His	Leu	Gly	Asn	Leu	Gln	Val	Leu	Arg	Leu	Tyr	Glu	Asn	Arg
	195						200					205			
Leu	Thr	Asp	Ile	Pro	Met	Gly	Thr	Phe	Asp	Gly	Leu	Val	Asn	Leu	Gln
	210					215					220				
Glu	Leu	Ala	Leu	Gln	Gln	Asn	Gln	Ile	Gly	Leu	Leu	Ser	Pro	Gly	Leu
225				230						235				240	
Phe	His	Asn	Asn	His	Asn	Leu	Gln	Arg	Leu	Tyr	Leu	Ser	Asn	Asn	His
			245						250					255	
Ile	Ser	Gln	Leu	Pro	Pro	Ser	Ile	Phe	Met	Gln	Leu	Pro	Gln	Leu	Asn
		260						265					270		
Arg	Leu	Thr	Leu	Phe	Gly	Asn	Ser	Leu	Lys	Glu	Leu	Ser	Leu	Gly	Ile
	275					280						285			
Phe	Gly	Pro	Met	Pro	Asn	Leu	Arg	Glu	Leu	Trp	Leu	Tyr	Asp	Asn	His

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      290              295              300
Ile Ser Ser Leu Pro Asp Asn Val Phe Ser Asn Leu Arg Gln Leu Gln
305              310              315              320
Val Leu Ile Leu Ser Arg Asn Gln Ile Ser Phe Ile Ser Pro Gly Ala
              325              330              335
Phe Asn Gly Leu Thr Glu Leu Arg Glu Leu Ser Leu His Thr Asn Ala
              340              345              350
Leu Gln Asp Leu Asp Gly Asn Val Phe Arg Met Leu Ala Asn Leu Gln
              355              360              365
Asn Ile Ser Leu Gln Asn Asn Arg Leu Arg Gln Leu Pro Gly Asn Ile
              370              375              380
Phe Ala Asn Val Asn Gly Leu Met Ala Ile Gln Leu Gln Asn Asn Gln
              385              390              395              400
Leu Glu Asn Leu Pro Leu Gly Ile Phe Asp His Leu Gly Lys Leu Cys
              405              410              415
Glu Leu Arg Leu Tyr Asp Asn Pro Trp Arg Cys Asp Ser Asp Ile Leu
              420              425              430
Pro Leu Arg Asn Trp Leu Leu Leu Asn Gln Pro Arg Leu Gly Thr Asp
              435              440              445
Thr Val Pro Val Cys Phe Ser Pro Ala Asn Val Arg Gly Gln Ser Leu
              450              455              460
Ile Ile Ile Asn Val Asn Val Ala Val Pro Ser Val His Val Pro Glu
              465              470              475              480
Val Pro Ser Tyr Pro Glu Thr Pro Trp Tyr Pro Asp Thr Pro Ser Tyr
              485              490              495
Pro Asp Thr Thr Ser Val Ser Ser Thr Thr Glu Leu Thr Ser Pro Val
              500              505              510
Glu Asp Tyr Thr Asp Leu Thr Thr Ile Gln Val Thr Asp Asp Arg Ser
              515              520              525
Val Trp Gly Met Thr His Ala His Ser Gly Leu Ala Ile Ala Ala Ile
              530              535              540
Val Ile Gly Ile Val Ala Leu Ala Cys Ser Leu Ala Ala Cys Val Gly
              545              550              555              560
Cys Cys Cys Cys Lys Lys Arg Ser Gln Ala Val Leu Met Gln Met Lys
              565              570              575
Ala Pro Asn Glu Cys
              580

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&lt;210&gt; 44

&lt;211&gt; 628

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 44

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Met Pro Gly Ala Pro Asp Trp Ser Leu Asn Ser Ser Arg Asn Ala Arg
1              5              10              15
Ser Leu Glu Gly Leu Pro Leu Cys Pro Trp Trp Ala Leu Phe Val Pro
              20              25              30
Arg Ala Ala Ala Leu Val Gly Leu Gln Arg Lys Gln Glu Asn Ser Ser
              35              40              45
Asp Ile Phe Phe Ser Ser Pro Phe Thr Val Thr Pro Asp Ala Leu Pro
              50              55              60
Thr Ala Ile Thr Trp Glu His Ile Pro Phe Ala Lys Leu Ala Gly Leu
              65              70              75              80
Ile Ala Gly Pro Leu Val Glu Met Cys Arg Gln Arg Leu Ser Lys Glu
              85              90              95
Phe Glu Ala Leu Lys Gly Glu Phe Arg Asp Leu Gly His Cys Leu Pro
              100              105              110
Gly Ala Gln Arg Gly Asn Arg Ile Thr Lys Arg Asn Lys Cys Gly Gln

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		115					120					125			
Ser	Arg	Gln	Ala	Leu	Ile	Gly	Gln	Arg	Gln	Glu	Asp	Ala	Gly	Ser	Ala
	130					135					140				
Pro	Leu	Gln	Met	His	Pro	Ser	Val	Ala	Ala	Leu	Gly	Ala	Gly	Ala	Ala
145					150					155					160
Leu	Arg	Glu	Ile	Gln	Pro	Leu	Gln	Arg	Glu	Pro	Glu	Leu	Ser	Ser	Gly
				165					170					175	
Pro	Arg	Asn	Ser	Arg	Leu	Leu	Cys	Trp	Gly	Ser	Pro	Ala	Thr	Trp	Asn
			180					185					190		
Pro	Thr	Tyr	Leu	Ser	Arg	Val	Leu	Gly	Gln	Gln	Val	Ala	Val	Thr	Val
		195				200						205			
Thr	Glu	Ala	Gly	Leu	Gln	Ala	Val	Pro	Trp	Gly	Pro	Ser	Arg	Glu	Phe
	210					215					220				
Asn	Ala	Lys	Gly	Ser	Ser	Ser	Ala	Ser	Ile	Arg	Val	Gly	Gln	Pro	Gln
225					230					235					240
Lys	Leu	Arg	Leu	Arg	Val	Gln	Arg	Ser	Arg	Arg	Gln	Cys	Pro	Pro	Val
				245					250					255	
Gln	Ser	Ser	Gln	Asp	Leu	Pro	Pro	Gly	Gly	Ser	Gln	Asp	Gly	Asp	Leu
			260					265					270		
Lys	Glu	Pro	Thr	Glu	Arg	Val	Thr	Arg	Asp	Leu	Ser	Ser	Gly	Ala	Pro
		275				280						285			
Arg	Gly	Arg	Asn	Leu	Pro	Ala	Pro	Asp	Gln	Pro	Gln	Pro	Pro	Leu	Gln
	290					295					300				
Arg	Gly	Thr	Arg	Leu	Arg	Leu	Arg	Gln	Arg	Arg	Arg	Arg	Leu	Leu	Ile
305				310						315					320
Lys	Lys	Met	Pro	Ala	Ala	Ala	Thr	Ile	Pro	Ala	Asn	Ser	Ser	Asp	Ala
			325						330					335	
Pro	Phe	Ile	Arg	Pro	Gly	Pro	Gly	Thr	Leu	Asp	Gly	Arg	Trp	Val	Ser
			340					345					350		
Leu	His	Arg	Ser	Gln	Gln	Glu	Arg	Lys	Arg	Val	Met	Gln	Glu	Ala	Cys
		355					360					365			
Ala	Lys	Tyr	Arg	Ala	Ser	Ser	Ser	Arg	Arg	Ala	Val	Thr	Pro	Arg	His
	370					375					380				
Val	Ser	Arg	Ile	Phe	Val	Glu	Asp	Arg	His	Arg	Val	Leu	Tyr	Cys	Glu
385				390						395					400
Val	Pro	Lys	Ala	Gly	Cys	Ser	Asn	Trp	Lys	Arg	Val	Leu	Met	Val	Leu
			405						410					415	
Ala	Gly	Leu	Ala	Ser	Ser	Thr	Ala	Asp	Ile	Gln	His	Asn	Thr	Val	His
			420					425					430		
Tyr	Gly	Ser	Ala	Leu	Lys	Arg	Leu	Asp	Thr	Phe	Asp	Arg	Gln	Gly	Ile
		435					440					445			
Leu	His	Arg	Leu	Ser	Thr	Tyr	Thr	Lys	Met	Leu	Phe	Val	Arg	Glu	Pro
	450					455					460				
Phe	Glu	Arg	Leu	Val	Ser	Ala	Phe	Arg	Asp	Lys	Phe	Glu	His	Pro	Asn
465				470											

His Gln Tyr Phe Ala Gln Leu Ser Ala Leu Gln Arg Gln Arg Thr Tyr  
 595 600 605  
 Asp Phe Tyr Tyr Met Asp Tyr Leu Met Phe Asn Tyr Ser Lys Pro Phe  
 610 615 620  
 Ala Asp Leu Tyr  
 625

<210> 45  
 <211> 424  
 <212> PRT  
 <213> Homo sapiens

<400> 45  
 Met Thr Leu Arg Pro Gly Thr Met Arg Leu Ala Cys Met Phe Ser Ser  
 1 5 10 15  
 Ile Leu Leu Phe Gly Ala Ala Gly Leu Leu Leu Phe Ile Ser Leu Gln  
 20 25 30  
 Asp Pro Thr Glu Leu Ala Pro Gln Gln Val Pro Gly Ile Lys Phe Asn  
 35 40 45  
 Ile Arg Pro Arg Gln Pro His His Asp Leu Pro Pro Gly Gly Ser Gln  
 50 55 60  
 Asp Gly Asp Leu Lys Glu Pro Thr Glu Arg Val Thr Arg Asp Leu Ser  
 65 70 75 80  
 Ser Gly Ala Pro Arg Gly Arg Asn Leu Pro Ala Pro Asp Gln Pro Gln  
 85 90 95  
 Pro Pro Leu Gln Arg Gly Thr Arg Leu Arg Leu Arg Gln Arg Arg Arg  
 100 105 110  
 Arg Leu Leu Ile Lys Lys Met Pro Ala Ala Ala Thr Ile Pro Ala Asn  
 115 120 125  
 Ser Ser Asp Ala Pro Phe Ile Arg Pro Gly Pro Gly Thr Leu Asp Gly  
 130 135 140  
 Arg Trp Val Ser Leu His Arg Ser Gln Gln Glu Arg Lys Arg Val Met  
 145 150 155 160  
 Gln Glu Ala Cys Ala Lys Tyr Arg Ala Ser Ser Ser Arg Arg Ala Val  
 165 170 175  
 Thr Pro Arg His Val Ser Arg Ile Phe Val Glu Asp Arg His Arg Val  
 180 185 190  
 Leu Tyr Cys Glu Val Pro Lys Ala Gly Cys Ser Asn Trp Lys Arg Val  
 195 200 205  
 Leu Met Val Leu Ala Gly Leu Ala Ser Ser Thr Ala Asp Ile Gln His  
 210 215 220  
 Asn Thr Val His Tyr Gly Ser Ala Leu Lys Arg Leu Asp Thr Phe Asp  
 225 230 235 240  
 Arg Gln Gly Ile Leu His Arg Leu Ser Thr Tyr Thr Lys Met Leu Phe  
 245 250 255  
 Val Arg Glu Pro Phe Glu Arg Leu Val Ser Ala Phe Arg Asp Lys Phe  
 260 265 270  
 Glu His Pro Asn Ser Tyr Tyr His Pro Val Phe Gly Lys Ala Ile Leu  
 275 280 285  
 Ala Arg Tyr Arg Ala Asn Ala Ser Arg Glu Ala Leu Arg Thr Gly Ser  
 290 295 300  
 Gly Val Arg Phe Pro Glu Phe Val Gln Tyr Leu Leu Asp Val His Arg  
 305 310 315 320  
 Pro Val Gly Met Asp Ile His Trp Asp His Val Ser Arg Leu Cys Ser  
 325 330 335  
 Pro Cys Leu Ile Asp Tyr Asp Phe Val Gly Lys Phe Glu Ser Met Glu  
 340 345 350  
 Asp Asp Ala Asn Phe Phe Leu Ser Leu Ile Arg Ala Pro Arg Asn Leu  
 355 360 365

Thr Phe Pro Arg Phe Lys Asp Arg His Ser Gln Glu Ala Arg Thr Thr  
 370 375 380  
 Ala Arg Ile Ala His Gln Tyr Phe Ala Gln Leu Ser Ala Leu Gln Arg  
 385 390 395 400  
 Gln Arg Thr Tyr Asp Phe Tyr Tyr Met Asp Tyr Leu Met Phe Asn Tyr  
 405 410 415  
 Ser Lys Pro Phe Ala Asp Leu Tyr  
 420

<210> 46  
 <211> 638  
 <212> PRT  
 <213> Homo sapiens

<400> 46  
 Met Ala Gly Gly Ser Ala Thr Thr Trp Gly Tyr Pro Val Ala Leu Leu  
 1 5 10 15  
 Leu Leu Val Ala Thr Leu Gly Leu Gly Arg Trp Leu Gln Pro Asp Pro  
 20 25 30  
 Gly Leu Pro Gly Leu Arg His Ser Tyr Asp Cys Gly Ile Lys Gly Met  
 35 40 45  
 Gln Leu Leu Val Phe Pro Arg Pro Gly Gln Thr Leu Arg Phe Lys Val  
 50 55 60  
 Val Asp Glu Phe Gly Asn Arg Phe Asp Val Asn Asn Cys Ser Ile Cys  
 65 70 75 80  
 Tyr His Trp Val Thr Ser Arg Pro Gln Glu Pro Ala Val Phe Ser Ala  
 85 90 95  
 Asp Tyr Arg Gly Cys His Val Leu Glu Lys Asp Gly Arg Phe His Leu  
 100 105 110  
 Arg Val Phe Met Glu Ala Val Leu Pro Asn Gly Arg Val Asp Val Ala  
 115 120 125  
 Gln Asp Ala Thr Leu Ile Cys Pro Lys Pro Asp Pro Ser Arg Thr Leu  
 130 135 140  
 Asp Ser Gln Leu Ala Pro Pro Ala Met Phe Ser Val Ser Thr Pro Gln  
 145 150 155 160  
 Thr Leu Ser Phe Leu Pro Thr Ser Gly His Thr Ser Gln Gly Ser Gly  
 165 170 175  
 His Ala Phe Pro Ser Pro Leu Asp Pro Gly His Ser Ser Val His Pro  
 180 185 190  
 Thr Pro Ala Leu Pro Ser Pro Gly Pro Gly Pro Thr Leu Ala Thr Leu  
 195 200 205  
 Ala Gln Pro His Trp Gly Thr Leu Glu His Trp Asp Val Asn Lys Arg  
 210 215 220  
 Asp Tyr Ile Gly Thr His Leu Ser Gln Glu Gln Cys Gln Val Ala Ser  
 225 230 235 240  
 Gly His Leu Pro Cys Ile Val Arg Arg Thr Ser Lys Glu Ala Cys Gln  
 245 250 255  
 Gln Ala Gly Cys Cys Tyr Asp Asn Thr Arg Glu Val Pro Cys Tyr Tyr  
 260 265 270  
 Gly Asn Thr Ala Thr Val Gln Cys Phe Arg Asp Gly Tyr Phe Val Leu  
 275 280 285  
 Val Val Ser Gln Glu Met Ala Leu Thr His Arg Ile Thr Leu Ala Asn  
 290 295 300  
 Ile His Leu Ala Tyr Ala Pro Thr Ser Cys Ser Pro Thr Gln His Thr  
 305 310 315 320  
 Glu Ala Phe Val Val Phe Tyr Phe Pro Leu Thr His Cys Gly Thr Thr  
 325 330 335  
 Met Gln Val Ala Gly Asp Gln Leu Ile Tyr Glu Asn Trp Leu Val Ser  
 340 345 350

Gly Ile His Ile Gln Lys Gly Pro Gln Gly Ser Ile Thr Arg Asp Ser  
 355 360 365  
 Thr Phe Gln Leu His Val Arg Cys Val Phe Asn Ala Ser Asp Phe Leu  
 370 375 380  
 Pro Ile Gln Ala Ser Ile Phe Pro Pro Pro Ser Pro Ala Pro Met Thr  
 385 390 395 400  
 Gln Pro Gly Pro Leu Arg Leu Glu Leu Arg Ile Ala Lys Asp Glu Thr  
 405 410 415  
 Phe Ser Ser Tyr Tyr Gly Glu Asp Asp Tyr Pro Ile Val Arg Leu Leu  
 420 425 430  
 Arg Glu Pro Val His Val Glu Val Arg Leu Leu Gln Arg Thr Asp Pro  
 435 440 445  
 Asn Leu Val Leu Leu Leu His Gln Cys Trp Gly Ala Pro Ser Ala Asn  
 450 455 460  
 Pro Phe Gln Gln Pro Gln Trp Pro Ile Leu Ser Asp Gly Cys Pro Phe  
 465 470 475 480  
 Lys Gly Asp Ser Tyr Arg Thr Gln Met Val Ala Leu Asp Gly Ala Thr  
 485 490 495  
 Pro Phe Gln Ser His Tyr Gln Arg Phe Thr Val Ala Thr Phe Ala Leu  
 500 505 510  
 Leu Asp Ser Gly Ser Gln Arg Ala Leu Arg Gly Leu Val Tyr Leu Phe  
 515 520 525  
 Cys Ser Thr Ser Ala Cys His Thr Ser Gly Leu Glu Thr Cys Ser Thr  
 530 535 540  
 Ala Cys Ser Thr Gly Thr Thr Arg Gln Arg Arg Ser Ser Gly His Arg  
 545 550 555 560  
 Asn Asp Thr Ala Arg Pro Gln Asp Ile Val Ser Ser Pro Gly Pro Val  
 565 570 575  
 Gly Phe Glu Asp Ser Tyr Gly Gln Glu Pro Thr Leu Gly Pro Thr Asp  
 580 585 590  
 Ser Asn Gly Asn Ser Ser Leu Arg Pro Leu Leu Trp Ala Val Leu Leu  
 595 600 605  
 Leu Pro Ala Val Ala Leu Val Leu Gly Phe Gly Val Phe Val Gly Leu  
 610 615 620  
 Ser Gln Thr Trp Ala Gln Lys Leu Trp Glu Ser Asn Arg Gln  
 625 630 635

&lt;210&gt; 47

&lt;211&gt; 229

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

Met Lys Pro Leu Ala Gln Leu Leu Leu Phe Leu Leu Gln Phe Gln Lys  
 1 5 10 15  
 Gly Asn Leu Val Ser Gln Ser Ser Ser Thr Pro Leu Met Val Asn Gly  
 20 25 30  
 Val Leu Gly Glu Ser Val Thr Leu Pro Leu Glu Phe Pro Ala Gly Glu  
 35 40 45  
 Arg Ile Gln Phe Ile Thr Trp Leu Cys Asn Gly Thr Ser Phe Ala Phe  
 50 55 60  
 Leu Glu Pro Tyr Glu Gly Lys Ser Pro Lys Ile Tyr Val Thr His Pro  
 65 70 75 80  
 Lys Trp Gln Lys Arg Leu Ser Phe Thr Gln Ser Tyr Ser Pro Gln Leu  
 85 90 95  
 Ser Asn Leu Glu Met Glu Asn Ile Gly Phe Tyr Ser Ala Gln Ile Ala  
 100 105 110  
 Thr Glu Thr Ser Ala Lys Leu Ser Ser Tyr Thr Leu Arg Ile Phe Lys  
 115 120 125

Gln Leu Pro Arg Pro Gln Val Arg Val Asp Ser Ile Ile Ser Glu Asn  
 130 135 140  
 Gly Ile Cys Asn Ala Ile Leu Arg Cys Ser Val Glu Glu Gly Gly Glu  
 145 150 155 160  
 Thr Ile Thr Tyr Glu Trp Thr Ser Met Gly Pro Gly Ala Ala Val Ser  
 165 170 175  
 His Val Gly Leu His Asp Leu Asp Trp Ile Tyr Thr Cys Thr Ala Leu  
 180 185 190  
 Asn Pro Val Ser Tyr Ser Asn Ser Thr Leu Thr Leu Ala Ala Gln Leu  
 195 200 205  
 Cys Ala Ser Lys Ser Pro Leu Leu Val Ser Leu Ala Pro Leu Gly Asn  
 210 215 220  
 Val Leu Ser Gly Leu  
 225

<210> 48  
 <211> 310  
 <212> PRT  
 <213> Homo sapiens

<400> 48  
 Met Lys Pro Leu Ala Gln Leu Leu Leu Phe Leu Leu Gln Phe Gln Lys  
 1 5 10 15  
 Gly Asn Leu Val Ser Gln Ser Ser Ser Thr Pro Leu Met Val Asn Gly  
 20 25 30  
 Val Leu Gly Glu Ser Val Thr Leu Pro Leu Glu Phe Pro Ala Gly Glu  
 35 40 45  
 Arg Ile Gln Phe Ile Thr Trp Leu Cys Asn Gly Thr Ser Phe Ala Phe  
 50 55 60  
 Leu Glu Pro Tyr Glu Gly Lys Ser Pro Lys Ile Tyr Val Thr His Pro  
 65 70 75 80  
 Lys Trp Gln Lys Arg Leu Ser Phe Thr Gln Ser Tyr Ser Pro Gln Leu  
 85 90 95  
 Ser Asn Leu Glu Met Glu Asn Ile Gly Phe Tyr Ser Ala Gln Ile Ala  
 100 105 110  
 Thr Glu Thr Ser Ala Lys Leu Ser Ser Tyr Thr Leu Arg Ile Phe Lys  
 115 120 125  
 Gln Leu Pro Arg Pro Gln Val Arg Val Asp Ser Ile Ile Ser Glu Asn  
 130 135 140  
 Gly Ile Cys Asn Ala Ile Leu Arg Cys Ser Val Glu Glu Gly Gly Glu  
 145 150 155 160  
 Thr Ile Thr Tyr Glu Trp Thr Ser Met Gly Pro Gly Ala Ala Val Ser  
 165 170 175  
 His Val Gly Leu His Asp Leu Asp Trp Ile Tyr Thr Cys Thr Ala Leu  
 180 185 190  
 Asn Pro Val Ser Tyr Ser Asn Ser Thr Leu Thr Leu Ala Ala Gln Leu  
 195 200 205  
 Cys Ala Ser Ser Lys Ala Ala Glu Gly Thr Tyr Cys Pro Val Lys Trp  
 210 215 220  
 Ile Phe Leu Gly Asn Arg Leu Leu Leu Leu Val Phe Leu Gly Val Leu  
 225 230 235 240  
 Arg Thr Trp His Ile Gln Ala Gln Val Leu Ser Lys Pro Leu Arg Pro  
 245 250 255  
 Asn Ser Gly Glu Leu Val Asn Leu Ser Ser Ile Pro Tyr Pro Trp Glu  
 260 265 270  
 Pro Ser His Thr Ala Asp Ala Thr Trp Leu Gly Lys Trp Gly Gly Ser  
 275 280 285  
 Glu Gly Glu Arg Lys Ser Thr Trp Asn Ile Ser Thr Thr Lys Arg His  
 290 295 300



Trp Lys Ser Phe Tyr Lys  
305 310

<210> 49  
<211> 841  
<212> PRT  
<213> Homo sapiens

<400> 49  
Met Lys Leu Trp Ile His Leu Phe Tyr Ser Ser Leu Leu Ala Cys Ile  
1 5 10 15  
Ser Leu His Ser Gln Thr Pro Val Leu Ser Ser Arg Gly Ser Cys Asp  
20 25 30  
Ser Leu Cys Asn Cys Glu Glu Lys Asp Gly Thr Met Leu Ile Asn Cys  
35 40 45  
Glu Ala Lys Gly Ile Lys Met Val Ser Glu Ile Ser Val Pro Pro Ser  
50 55 60  
Arg Pro Phe Gln Leu Ser Leu Leu Asn Asn Gly Leu Thr Met Leu His  
65 70 75 80  
Thr Asn Asp Phe Ser Gly Leu Thr Asn Ala Ile Ser Ile His Leu Gly  
85 90 95  
Phe Asn Asn Ile Ala Asp Ile Glu Ile Gly Ala Phe Asn Gly Leu Gly  
100 105 110  
Leu Leu Lys Gln Leu His Ile Asn His Asn Ser Leu Glu Ile Leu Lys  
115 120 125  
Glu Asp Thr Phe His Gly Leu Glu Asn Leu Glu Phe Leu Gln Ala Asp  
130 135 140  
Asn Asn Phe Ile Thr Val Ile Glu Pro Ser Ala Phe Ser Lys Leu Asn  
145 150 155 160  
Arg Leu Lys Val Leu Ile Leu Asn Asp Asn Ala Ile Glu Ser Leu Pro  
165 170 175  
Pro Asn Ile Phe Arg Phe Val Pro Leu Thr His Leu Asp Leu Arg Gly  
180 185 190  
Asn Gln Leu Gln Thr Leu Pro Tyr Val Gly Phe Leu Glu His Ile Gly  
195 200 205  
Arg Ile Leu Asp Leu Gln Leu Glu Asp Asn Lys Trp Ala Cys Asn Cys  
210 215 220  
Asp Leu Leu Gln Leu Lys Thr Trp Leu Glu Asn Met Pro Pro Gln Ser  
225 230 235 240  
Ile Ile Gly Asp Val Val Cys Asn Ser Pro Phe Phe Lys Gly Ser  
245 250 255  
Ile Leu Ser Arg Leu Lys Lys Glu Ser Ile Cys Pro Thr Pro Pro Val  
260 265 270  
Tyr Glu Glu His Glu Asp Pro Ser Gly Ser Leu His Leu Ala Ala Thr  
275 280 285  
Ser Ser Ile Asn Asp Ser Arg Met Ser Thr Lys Thr Thr Ser Ile Leu  
290 295 300  
Lys Leu Pro Thr Lys Ala Pro Gly Leu Ile Pro Tyr Ile Thr Lys Pro  
305 310 315 320  
Ser Thr Gln Leu Pro Gly Pro Tyr Cys Pro Ile Pro Cys Asn Cys Lys  
325 330 335  
Val Leu Ser Pro Ser Gly Leu Leu Ile His Cys Gln Glu Arg Asn Ile  
340 345 350  
Glu Ser Leu Ser Asp Leu Arg Pro Pro Pro Gln Asn Pro Arg Lys Leu  
355 360 365  
Ile Leu Ala Gly Asn Ile Ile His Ser Leu Met Lys Ser Asp Leu Val  
370 375 380  
Glu Tyr Phe Thr Leu Glu Met Leu His Leu Gly Asn Asn Arg Ile Glu  
385 390 395 400

Val Leu Glu Glu Gly Ser Phe Met Asn Leu Thr Arg Leu Gln Lys Leu  
 405 410 415  
 Tyr Leu Asn Gly Asn His Leu Thr Lys Leu Ser Lys Gly Met Phe Leu  
 420 425 430  
 Gly Leu His Asn Leu Glu Tyr Leu Tyr Leu Glu Tyr Asn Ala Ile Lys  
 435 440 445  
 Glu Ile Leu Pro Gly Thr Phe Asn Pro Met Pro Lys Leu Lys Val Leu  
 450 455 460  
 Tyr Leu Asn Asn Asn Leu Leu Gln Val Leu Pro Pro His Ile Phe Ser  
 465 470 475 480  
 Gly Val Pro Leu Thr Lys Val Asn Leu Lys Thr Asn Gln Phe Thr His  
 485 490 495  
 Leu Pro Val Ser Asn Ile Leu Asp Asp Leu Asp Leu Leu Thr Gln Ile  
 500 505 510  
 Asp Leu Glu Asp Asn Pro Trp Asp Cys Ser Cys Asp Leu Val Gly Leu  
 515 520 525  
 Gln Gln Trp Ile Gln Lys Leu Ser Lys Asn Thr Val Thr Asp Asp Ile  
 530 535 540  
 Leu Cys Thr Ser Pro Gly His Leu Asp Lys Lys Glu Leu Lys Ala Leu  
 545 550 555 560  
 Asn Ser Glu Ile Leu Cys Pro Gly Leu Val Asn Asn Pro Ser Met Pro  
 565 570 575  
 Thr Gln Thr Ser Tyr Leu Met Val Thr Thr Pro Ala Thr Thr Thr Asn  
 580 585 590  
 Thr Ala Asp Thr Ile Leu Arg Ser Leu Thr Asp Ala Val Pro Leu Ser  
 595 600 605  
 Val Leu Ile Leu Gly Leu Leu Ile Met Phe Ile Thr Ile Val Phe Cys  
 610 615 620  
 Ala Ala Gly Ile Val Val Leu Val Leu His Arg Arg Arg Arg Tyr Lys  
 625 630 635 640  
 Lys Lys Gln Val Asp Glu Gln Met Arg Asp Asn Ser Pro Val His Leu  
 645 650 655  
 Gln Tyr Ser Met Tyr Gly His Lys Thr Thr His His Thr Thr Glu Arg  
 660 665 670  
 Pro Ser Ala Ser Leu Tyr Glu Gln His Met Val Ser Pro Met Val His  
 675 680 685  
 Val Tyr Arg Ser Pro Ser Phe Gly Pro Lys His Leu Glu Glu Glu Glu  
 690 695 700  
 Glu Arg Asn Glu Lys Glu Gly Ser Asp Ala Lys His Leu Gln Arg Ser  
 705 710 715 720  
 Leu Leu Glu Gln Glu Asn His Ser Pro Leu Thr Gly Ser Asn Met Lys  
 725 730 735  
 Tyr Lys Thr Thr Asn Gln Ser Thr Glu Phe Leu Ser Phe Gln Asp Ala  
 740 745 750  
 Ser Ser Leu Tyr Arg Asn Ile Leu Glu Lys Glu Arg Glu Leu Gln Gln  
 755 760 765  
 Leu Gly Ile Thr Glu Tyr Leu Arg Lys Asn Ile Ala Gln Leu Gln Pro  
 770 775 780  
 Asp Met Glu Ala His Tyr Pro Gly Ala His Glu Glu Leu Lys Leu Met  
 785 790 795 800  
 Glu Thr Leu Met Tyr Ser Arg Pro Arg Lys Val Leu Val Glu Gln Thr  
 805 810 815  
 Lys Asn Glu Tyr Phe Glu Leu Lys Ala Asn Leu His Ala Glu Pro Asp  
 820 825 830  
 Tyr Leu Glu Val Leu Glu Gln Gln Thr  
 835 840

&lt;210&gt; 50

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

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Met Gly Asn Pro Gly Leu Ala Trp Leu Val Leu Leu Gly Leu Val Leu
 1           5           10           15
Leu Leu Ser Ser Phe Met Glu Arg Gly Gly His Ser Pro Ser Pro Ala
 20           25           30
Ala Leu Ser Ala Met Glu Asn Leu Ile Thr Tyr Ala Val Gln Lys Gly
 35           40           45
His Leu Ser Ser Ser Tyr Val Gln Pro Leu Leu Val Lys Gly Glu Asn
 50           55           60
Cys Leu Ala Pro Arg Gln Lys Thr Ser Leu Lys Lys Ala Cys Pro Gly
 65           70           75           80
Val Val Pro Arg Ser Val Trp Gly Ala Arg Glu Thr His Cys Pro Arg
 85           90           95
Met Thr Leu Pro Ala Lys Tyr Gly Ile Ile Ile His Thr Ala Gly Arg
 100          105          110
Thr Cys Asn Ile Ser Asp Glu Cys Arg Leu Leu Val Arg Asp Ile Gln
 115          120          125
Ser Phe Tyr Ile Asp Arg Leu Lys Ser Cys Asp Ile Gly Tyr Asn Phe
 130          135          140
Leu Val Gly Gln Asp Gly Ala Ile Tyr Glu Gly Val Gly Trp Asn Val
 145          150          155          160
Gln Gly Ser Ser Thr Pro Gly Tyr Asp Asp Ile Ala Leu Gly Ile Thr
 165          170          175
Phe Met Gly Thr Phe Thr Gly Ile Pro Pro Asn Ala Ala Ala Leu Glu
 180          185          190
Ala Ala Gln Asp Leu Ile Gln Cys Ala Met Val Lys Gly Tyr Leu Thr
 195          200          205
Pro Asn Tyr Leu Leu Val Gly His Ser Asp Val Ala Arg Thr Leu Ser
 210          215          220
Pro Gly Gln Ala Leu Tyr Asn Ile Ile Ser Thr Trp Pro His Phe Lys
 225          230          235          240
His

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&lt;210&gt; 51

&lt;211&gt; 369

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 51

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Met Leu Pro Trp Leu Leu Val Phe Ser Ala Leu Gly Leu Gln Ala Trp
 1           5           10           15
Gly Asp Ser Ser Trp Asn Lys Thr Gln Ala Lys Gln Val Ser Glu Gly
 20           25           30
Leu Gln Tyr Leu Phe Glu Asn Ile Ser Gln Leu Thr Glu Lys Asp Val
 35           40           45
Ser Thr Thr Val Ser Arg Lys Ala Trp Gly Ala Glu Ala Val Gly Cys
 50           55           60
Ser Ile Gln Leu Thr Thr Pro Val Asn Val Leu Val Ile His His Val
 65           70           75           80
Pro Gly Leu Glu Cys His Asp Arg Thr Val Cys Ser Gln Arg Leu Arg
 85           90           95
Glu Leu Gln Ala His His Val His Asn Asn Ser Gly Cys Asp Val Ala
 100          105          110
Tyr Asn Phe Leu Val Gly Asp Asp Gly Arg Val Tyr Glu Gly Val Gly
 115          120          125

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Trp Asn Ile Gln Gly Val His Thr Gln Gly Tyr Asn Asn Ile Ser Leu  
 130 135 140  
 Gly Phe Ala Phe Phe Gly Thr Lys Lys Gly His Ser Pro Ser Pro Ala  
 145 150 155 160  
 Ala Leu Ser Ala Met Glu Asn Leu Ile Thr Tyr Ala Val Gln Lys Gly  
 165 170 175  
 His Leu Ser Ser Ser Tyr Val Gln Pro Leu Leu Val Lys Gly Glu Asn  
 180 185 190  
 Cys Leu Ala Pro Arg Gln Lys Thr Ser Leu Lys Lys Ala Cys Pro Gly  
 195 200 205  
 Val Val Pro Arg Ser Val Trp Gly Ala Arg Glu Thr His Cys Pro Arg  
 210 215 220  
 Met Thr Leu Pro Ala Lys Tyr Gly Ile Ile Ile His Thr Ala Gly Arg  
 225 230 235 240  
 Thr Cys Asn Ile Ser Asp Glu Cys Arg Leu Leu Val Arg Asp Ile Gln  
 245 250 255  
 Ser Phe Tyr Ile Asp Arg Leu Lys Ser Cys Asp Ile Gly Tyr Asn Phe  
 260 265 270  
 Leu Val Gly Gln Asp Gly Ala Ile Tyr Glu Gly Val Gly Trp Asn Val  
 275 280 285  
 Gln Gly Ser Ser Thr Pro Gly Tyr Asp Asp Ile Ala Leu Gly Ile Thr  
 290 295 300  
 Phe Met Gly Thr Phe Thr Gly Ile Pro Pro Asn Ala Ala Ala Leu Glu  
 305 310 315 320  
 Ala Ala Gln Asp Leu Ile Gln Cys Ala Met Val Lys Gly Tyr Leu Thr  
 325 330 335  
 Pro Asn Tyr Leu Leu Val Gly His Ser Asp Val Ala Arg Thr Leu Ser  
 340 345 350  
 Pro Gly Gln Ala Leu Tyr Asn Ile Ile Ser Thr Trp Pro His Phe Lys  
 355 360 365  
 His

<210> 52  
 <211> 382  
 <212> PRT  
 <213> Homo sapiens

<400> 52  
 Met Ala Pro Arg Ala Gly Gln Pro Gly Leu Gln Gly Leu Leu Leu Val  
 1 5 10 15  
 Ala Ala Ala Leu Ser Gln Pro Ala Ala Pro Cys Pro Phe Gln Cys Tyr  
 20 25 30  
 Cys Phe Gly Gly Pro Lys Leu Leu Arg Cys Ala Ser Gly Ala Glu  
 35 40 45  
 Leu Arg Gln Pro Pro Arg Asp Val Pro Pro Asp Ala Arg Asn Leu Thr  
 50 55 60  
 Ile Val Gly Ala Asn Leu Thr Val Leu Arg Ala Ala Ala Phe Ala Gly  
 65 70 75 80  
 Gly Asp Gly Asp Gly Asp Gln Ala Ala Gly Val Arg Leu Pro Leu Leu  
 85 90 95  
 Ser Ala Leu Arg Leu Thr His Asn His Ile Glu Val Val Glu Asp Gly  
 100 105 110  
 Ala Phe Asp Gly Leu Pro Ser Leu Ala Ala Leu Asp Leu Ser His Asn  
 115 120 125  
 Pro Leu Arg Ala Leu Gly Gly Gly Ala Phe Arg Gly Leu Pro Ala Leu  
 130 135 140  
 Arg Ser Leu Gln Leu Asn His Ala Leu Val Arg Gly Gly Pro Ala Leu  
 145 150 155 160

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Leu Ala Ala Leu Asp Ala Ala Leu Ala Pro Leu Ala Glu Leu Arg Leu
      165      170      175
Leu Gly Leu Ala Gly Asn Ala Leu Ser Arg Leu Pro Pro Ala Ala Leu
      180      185      190
Arg Leu Ala Arg Leu Glu Gln Leu Asp Val Arg Leu Asn Ala Leu Ala
      195      200      205
Gly Leu Asp Pro Asp Glu Leu Arg Ala Leu Glu Arg Asp Gly Gly Leu
      210      215      220
Pro Gly Pro Arg Leu Leu Leu Ala Asp Asn Pro Leu Arg Cys Gly Cys
      225      230      235      240
Ala Ala Arg Pro Leu Leu Ala Trp Leu Arg Asn Ala Thr Glu Arg Val
      245      250      255
Pro Asp Ser Arg Arg Leu Arg Cys Ala Ala Pro Arg Ala Leu Leu Asp
      260      265      270
Arg Pro Leu Leu Asp Leu Asp Gly Ala Arg Leu Arg Cys Ala Asp Ser
      275      280      285
Gly Ala Asp Ala Arg Gly Glu Glu Ala Glu Ala Ala Gly Pro Glu Leu
      290      295      300
Glu Ala Ser Tyr Val Phe Phe Gly Leu Val Leu Ala Leu Ile Gly Leu
      305      310      315      320
Ile Phe Leu Met Val Leu Tyr Leu Asn Arg Arg Gly Ile Gln Arg Trp
      325      330      335
Met Arg Asn Leu Arg Glu Ala Cys Arg Asp Gln Met Glu Gly Tyr His
      340      345      350
Tyr Arg Tyr Glu Gln Asp Ala Asp Pro Arg Arg Ala Pro Ala Pro Ala
      355      360      365
Ala Pro Ala Gly Ser Arg Ala Thr Ser Pro Gly Ser Gly Leu
      370      375      380

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&lt;210&gt; 53

&lt;211&gt; 185

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 53

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Met Met Leu Leu Leu Leu Cys Leu Gly Leu Thr Leu Val Cys Ala Gln
  1      5      10      15
Glu Glu Glu Asn Asn Asp Ala Val Thr Ser Asn Phe Asp Leu Ser Lys
      20      25      30
Ile Ser Gly Glu Trp Tyr Ser Val Leu Leu Ala Ser Asp Cys Arg Glu
      35      40      45
Lys Ile Glu Glu Asp Gly Ser Met Arg Val Phe Val Lys His Ile Asp
      50      55      60
Tyr Leu Gly Asn Ser Ser Leu Thr Phe Lys Leu His Glu Ile Glu Asn
      65      70      75      80
Gly Asn Cys Thr Glu Ile Asn Leu Ala Cys Lys Pro Thr Glu Lys Asn
      85      90      95
Ala Ile Cys Ser Thr Asp Tyr Asn Gly Leu Asn Val Ile Asp Ile Leu
      100      105      110
Glu Thr Asp Tyr Asp Asn Tyr Ile Tyr Phe Tyr Asn Lys Asn Ile Lys
      115      120      125
Asn Gly Glu Thr Phe Leu Met Leu Glu Leu Tyr Val Arg Thr Pro Asp
      130      135      140
Val Ser Ser Gln Leu Lys Glu Arg Phe Val Lys Tyr Cys Glu Glu His
      145      150      155      160
Gly Ile Asp Lys Glu Asn Ile Phe Asp Leu Thr Lys Val Asp Arg Cys
      165      170      175
Leu Gln Ala Arg Asp Glu Gly Ala Ala
      180      185

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<210> 54  
 <211> 586  
 <212> PRT  
 <213> Homo sapiens

<400> 54  
 Met His Tyr Asn Leu Gln Gly Pro Thr Arg Arg Ile Arg Ile Ser Leu  
 1 5 10 15  
 Leu Asn Asp Gly Gly Leu Lys Ile Ala Asn Val Thr Lys Ala Asp Ala  
 20 25 30  
 Gly Thr Tyr Thr Cys Met Ala Glu Asn Gln Phe Gly Lys Ala Asn Gly  
 35 40 45  
 Thr Thr His Leu Val Val Thr Glu Pro Thr Arg Ile Thr Leu Ala Pro  
 50 55 60  
 Ser Asn Met Asp Val Ser Val Gly Glu Ser Val Ile Leu Pro Cys Gln  
 65 70 75 80  
 Val Gln His Asp Pro Leu Leu Asp Ile Ile Phe Thr Trp Tyr Phe Asn  
 85 90 95  
 Gly Ala Leu Ala Asp Phe Lys Lys Asp Gly Ser His Phe Glu Lys Val  
 100 105 110  
 Gly Gly Ser Ser Ser Gly Asp Leu Met Ile Arg Asn Ile Gln Leu Lys  
 115 120 125  
 His Ser Gly Lys Tyr Val Cys Met Val Gln Thr Gly Val Asp Ser Val  
 130 135 140  
 Ser Ser Ala Ala Asp Leu Ile Val Arg Gly Ser Pro Gly Pro Pro Glu  
 145 150 155 160  
 Asn Val Lys Val Asp Glu Ile Thr Asp Thr Thr Ala Gln Leu Ser Trp  
 165 170 175  
 Lys Glu Gly Lys Asp Asn His Ser Pro Val Ile Ser Tyr Ser Ile Gln  
 180 185 190  
 Ala Arg Thr Pro Phe Ser Val Gly Trp Gln Thr Val Thr Thr Val Pro  
 195 200 205  
 Glu Val Ile Asp Gly Lys Thr His Thr Ala Thr Val Val Glu Leu Asn  
 210 215 220  
 Pro Trp Val Glu Tyr Glu Phe Arg Val Val Ala Ser Asn Lys Ile Gly  
 225 230 235 240  
 Gly Gly Glu Pro Ser Leu Pro Ser Glu Lys Val Arg Thr Glu Glu Ala  
 245 250 255  
 Val Pro Glu Val Pro Pro Ser Glu Val Asn Gly Gly Gly Gly Ser Arg  
 260 265 270  
 Ser Glu Leu Val Ile Thr Trp Asp Pro Val Pro Glu Glu Leu Gln Asn  
 275 280 285  
 Gly Glu Gly Phe Gly Tyr Val Val Ala Phe Arg Pro Leu Gly Val Thr  
 290 295 300  
 Thr Trp Ile Gln Thr Val Val Thr Ser Pro Asp Thr Pro Arg Tyr Val  
 305 310 315 320  
 Phe Arg Asn Glu Ser Ile Val Pro Tyr Ser Pro Tyr Glu Val Lys Val  
 325 330 335  
 Gly Val Tyr Asn Asn Lys Gly Glu Gly Pro Phe Ser Pro Val Thr Thr  
 340 345 350  
 Val Phe Ser Ala Glu Glu Glu Pro Thr Val Ala Pro Ser Gln Val Ser  
 355 360 365  
 Ala Asn Ser Leu Ser Ser Ser Glu Ile Glu Val Ser Trp Asn Thr Ile  
 370 375 380  
 Pro Trp Lys Leu Ser Asn Gly His Leu Leu Gly Tyr Glu Val Arg Tyr  
 385 390 395 400  
 Trp Asn Gly Gly Gly Lys Glu Glu Ser Ser Ser Lys Met Lys Val Ala  
 405 410 415

Gly Asn Glu Thr Ser Ala Arg Leu Arg Gly Leu Lys Ser Asn Leu Ala  
 420 425 430  
 Tyr Tyr Thr Ala Val Arg Ala Tyr Asn Ser Ala Gly Ala Gly Pro Phe  
 435 440 445  
 Ser Ala Thr Val Asn Val Thr Thr Lys Lys Thr Pro Pro Ser Gln Pro  
 450 455 460  
 Pro Gly Asn Val Val Trp Asn Ala Thr Asp Thr Lys Val Leu Leu Asn  
 465 470 475 480  
 Trp Glu Gln Val Lys Ala Met Glu Asn Glu Ser Glu Val Thr Gly Tyr  
 485 490 495  
 Lys Val Phe Tyr Arg Thr Ser Ser Gln Asn Asn Val Gln Val Leu Asn  
 500 505 510  
 Thr Asn Lys Thr Ser Ala Glu Leu Val Leu Pro Ile Lys Glu Asp Tyr  
 515 520 525  
 Ile Ile Glu Val Lys Ala Thr Thr Asp Gly Gly Asp Gly Thr Ser Ser  
 530 535 540  
 Glu Gln Ile Arg Ile Pro Arg Ile Thr Ser Met Asp Ala Arg Gly Ser  
 545 550 555 560  
 Thr Ser Ala Ile Ser Asn Val His Pro Met Ser Ser Tyr Met Pro Ile  
 565 570 575  
 Val Leu Phe Leu Ile Val Tyr Val Leu Trp  
 580 585

<210> 55  
 <211> 1026  
 <212> PRT  
 <213> Homo sapiens

<400> 55  
 Met Leu Val Val Glu Arg Val Met Val Leu Pro Ile Gly Phe Pro Leu  
 1 5 10 15  
 Gly Val Ser Asp Asp Ser Thr Leu His Gly Pro Ile Phe Ile Gln Glu  
 20 25 30  
 Pro Ser Pro Val Met Phe Pro Leu Asp Ser Glu Glu Lys Lys Val Lys  
 35 40 45  
 Leu Asn Cys Glu Val Lys Gly Asn Pro Lys Pro His Ile Arg Trp Lys  
 50 55 60  
 Leu Asn Gly Thr Asp Val Asp Thr Gly Met Asp Phe Arg Tyr Ser Val  
 65 70 75 80  
 Val Glu Gly Ser Leu Leu Ile Asn Asn Pro Asn Lys Thr Gln Asp Ala  
 85 90 95  
 Gly Thr Tyr Gln Cys Thr Ala Thr Asn Ser Phe Gly Thr Ile Val Ser  
 100 105 110  
 Arg Glu Ala Lys Leu Gln Phe Ala Tyr Leu Asp Asn Phe Lys Thr Arg  
 115 120 125  
 Thr Arg Ser Thr Val Ser Val Arg Arg Gly Gln Gly Met Val Leu Leu  
 130 135 140  
 Cys Gly Pro Pro Pro His Ser Gly Glu Leu Ser Tyr Ala Trp Ile Phe  
 145 150 155 160  
 Asn Glu Tyr Pro Ser Tyr Gln Asp Asn Arg Arg Phe Val Ser Gln Glu  
 165 170 175  
 Thr Gly Asn Leu Tyr Ile Ala Lys Val Glu Lys Ser Asp Val Gly Asn  
 180 185 190  
 Tyr Thr Cys Val Val Thr Asn Thr Val Thr Asn His Lys Val Leu Gly  
 195 200 205  
 Pro Pro Thr Pro Leu Ile Leu Arg Asn Asp Gly Val Met Gly Glu Tyr  
 210 215 220  
 Glu Pro Lys Ile Glu Val Gln Phe Pro Glu Thr Val Pro Thr Ala Lys  
 225 230 235 240

Gly Ala Thr Val Lys Leu Glu Cys Phe Ala Leu Gly Asn Pro Val Pro  
 245 250 255  
 Thr Ile Ile Trp Arg Arg Ala Asp Gly Lys Pro Ile Ala Arg Lys Ala  
 260 265 270  
 Arg Arg His Lys Ser Asn Gly Ile Leu Glu Ile Pro Asn Phe Gln Gln  
 275 280 285  
 Glu Asp Ala Gly Leu Tyr Glu Cys Val Ala Glu Asn Ser Arg Gly Lys  
 290 295 300  
 Asn Val Ala Arg Gly Gln Leu Thr Phe Tyr Ala Gln Pro Asn Trp Ile  
 305 310 315 320  
 Gln Lys Ile Asn Asp Ile His Val Ala Met Glu Glu Asn Val Phe Trp  
 325 330 335  
 Glu Cys Lys Ala Asn Gly Arg Pro Lys Pro Thr Tyr Lys Trp Leu Lys  
 340 345 350  
 Asn Gly Glu Pro Leu Leu Thr Arg Asp Arg Ile Gln Ile Glu Gln Gly  
 355 360 365  
 Thr Leu Asn Ile Thr Ile Val Asn Leu Ser Asp Ala Gly Met Tyr Gln  
 370 375 380  
 Cys Leu Ala Glu Asn Lys His Gly Val Ile Phe Ser Asn Ala Glu Leu  
 385 390 395 400  
 Ser Val Ile Ala Val Gly Pro Asp Phe Ser Arg Thr Leu Leu Lys Arg  
 405 410 415  
 Val Thr Leu Val Lys Val Gly Gly Glu Val Val Ile Glu Cys Lys Pro  
 420 425 430  
 Lys Ala Ser Pro Lys Pro Val Tyr Thr Trp Lys Lys Gly Arg Asp Ile  
 435 440 445  
 Leu Lys Glu Asn Glu Arg Ile Thr Ile Ser Glu Asp Gly Asn Leu Arg  
 450 455 460  
 Ile Ile Asn Val Thr Lys Ser Asp Ala Gly Ser Tyr Thr Cys Ile Ala  
 465 470 475 480  
 Thr Asn His Phe Gly Thr Ala Ser Ser Thr Gly Asn Leu Val Val Lys  
 485 490 495  
 Asp Pro Thr Arg Val Met Val Pro Pro Ser Ser Met Asp Val Thr Val  
 500 505 510  
 Gly Glu Ser Ile Val Leu Pro Cys Gln Val Thr His Asp His Ser Leu  
 515 520 525  
 Asp Ile Val Phe Thr Trp Ser Phe Asn Gly His Leu Ile Asp Phe Asp  
 530 535 540  
 Arg Asp Gly Asp His Phe Glu Arg Val Gly Gly Asp Ser Ala Gly Asp  
 545 550 555 560  
 Leu Met Ile Arg Asn Ile Gln Leu Lys His Ala Gly Lys Tyr Val Cys  
 565 570 575  
 Met Val Gln Thr Ser Val Asp Arg Leu Ser Ala Ala Ala Asp Leu Ile  
 580 585 590  
 Val Arg Gly Pro Pro Gly Pro Pro Glu Ala Val Thr Ile Asp Glu Ile  
 595 600 605  
 Thr Asp Thr Thr Ala Gln Leu Ser Trp Arg Pro Gly Pro Asp Asn His  
 610 615 620  
 Ser Pro Ile Thr Met Tyr Val Ile Gln Ala Arg Thr Pro Phe Ser Val  
 625 630 635 640  
 Gly Trp Gln Ala Val Ser Thr Val Pro Glu Leu Ile Asp Gly Lys Thr  
 645 650 655  
 Phe Thr Ala Thr Val Val Gly Leu Asn Pro Trp Val Glu Tyr Glu Phe  
 660 665 670  
 Arg Thr Val Ala Ala Asn Val Ile Gly Ile Gly Glu Pro Ser Arg Pro  
 675 680 685  
 Ser Glu Lys Arg Arg Thr Glu Glu Ala Leu Pro Glu Val Thr Pro Ala  
 690 695 700  
 Asn Val Ser Gly Gly Gly Gly Ser Lys Ser Glu Leu Val Ile Thr Trp



705 710 715 720  
 Glu Thr Val Pro Glu Glu Leu Gln Asn Gly Arg Gly Phe Gly Tyr Val  
 725 730 735  
 Val Ala Phe Arg Pro Tyr Gly Lys Met Ile Trp Met Leu Thr Val Leu  
 740 745 750  
 Ala Ser Ala Asp Ala Ser Arg Tyr Val Phe Arg Asn Glu Ser Val His  
 755 760 765  
 Pro Phe Ser Pro Phe Glu Val Lys Val Gly Val Phe Asn Asn Lys Gly  
 770 775 780  
 Glu Gly Pro Phe Ser Pro Thr Thr Val Val Tyr Ser Ala Glu Glu Glu  
 785 790 795 800  
 Pro Thr Lys Pro Pro Ala Ser Ile Phe Ala Arg Ser Leu Ser Ala Thr  
 805 810 815  
 Asp Ile Glu Val Phe Trp Ala Ser Pro Leu Glu Lys Asn Arg Gly Arg  
 820 825 830  
 Ile Gln Gly Tyr Glu Val Lys Tyr Trp Arg His Glu Asp Lys Glu Glu  
 835 840 845  
 Asn Ala Arg Lys Ile Arg Thr Val Gly Asn Gln Thr Ser Thr Lys Ile  
 850 855 860  
 Thr Asn Leu Lys Gly Ser Val Leu Tyr His Leu Ala Val Lys Ala Tyr  
 865 870 875 880  
 Asn Ser Ala Gly Thr Gly Pro Ser Ser Ala Thr Val Asn Val Thr Thr  
 885 890 895  
 Arg Lys Pro Pro Pro Ser Gln Pro Pro Gly Asn Ile Ile Trp Asn Ser  
 900 905 910  
 Ser Asp Ser Lys Ile Ile Leu Asn Trp Asp Gln Val Lys Ala Leu Asp  
 915 920 925  
 Asn Glu Ser Glu Val Lys Gly Tyr Lys Val Leu Tyr Arg Trp Asn Arg  
 930 935 940  
 Gln Ser Ser Thr Ser Val Ile Glu Thr Asn Lys Thr Ser Val Glu Leu  
 945 950 955 960  
 Ser Leu Pro Phe Asp Glu Asp Tyr Ile Ile Glu Ile Lys Pro Phe Ser  
 965 970 975  
 Asp Gly Gly Asp Gly Ser Ser Ser Glu Gln Ile Arg Ile Pro Lys Ile  
 980 985 990  
 Ser Asn Ala Tyr Ala Arg Gly Ser Gly Ala Ser Thr Ser Asn Ala Cys  
 995 1000 1005  
 Thr Leu Ser Ala Ile Ser Thr Ile Met Ile Ser Leu Thr Ala Arg Ser  
 1010 1015 1020  
 Ser Leu  
 1025

<210> 56  
 <211> 844  
 <212> PRT  
 <213> Homo sapiens

<400> 56  
 Met Asp Asn Pro Gln Ala Leu Pro Leu Phe Leu Leu Leu Ala Ser Leu  
 1 5 10 15  
 Val Gly Ile Leu Thr Leu Arg Ala Ser Ser Gly Leu Gln Gln Thr Asn  
 20 25 30  
 Phe Ser Ser Ala Phe Ser Ser Asp Ser Lys Ser Ser Ser Gln Gly Leu  
 35 40 45  
 Gly Val Glu Val Pro Ser Ile Lys Pro Pro Ser Trp Lys Val Pro Asp  
 50 55 60  
 Gln Phe Leu Asp Ser Lys Ala Ser Ala Gly Ile Ser Asp Ser Ser Trp  
 65 70 75 80  
 Phe Pro Glu Ala Leu Ser Ser Asn Met Ser Gly Ser Phe Trp Ser Asn

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Cys Leu Ala Arg His Leu Val Ala Thr Arg Thr Cys Thr Val Thr Pro  
 565 570 575  
 Glu Ala Pro Arg Glu Val Leu Leu His Pro Leu Val Ala Glu Thr Arg  
 580 585 590  
 Leu Gly Glu Ala Glu Val Ala Leu Glu Ala Ser Gly Cys Pro Pro Pro  
 595 600 605  
 Ser Arg Ala Ser Trp Ala Arg Glu Gly Arg Pro Leu Ala Pro Gly Gly  
 610 615 620  
 Gly Ser Arg Leu Arg Leu Ser Gln Asp Gly Arg Lys Leu His Ile Gly  
 625 630 635 640  
 Asn Phe Ser Leu Asp Trp Asp Leu Gly Asn Tyr Ser Val Leu Cys Ser  
 645 650 655  
 Gly Ala Leu Gly Ala Gly Gly Asp Gln Ile Thr Leu Ile Asp Gly Pro  
 660 665 670  
 Ala Leu Gly Arg Thr Ser Thr Tyr Arg Asp Trp Val Ser Leu Leu Ile  
 675 680 685  
 Leu Gly Pro Gln Glu Arg Ser Ala Val Val Pro Leu Pro Pro Arg Asn  
 690 695 700  
 Pro Gly Thr Trp Thr Phe Arg Ile Leu Pro Ile Leu Gly Gly Gln Pro  
 705 710 715 720  
 Gly Thr Pro Ser Gln Ser Arg Val Tyr Arg Ala Gly Pro Thr Leu Ser  
 725 730 735  
 His Gly Ala Ile Ala Gly Ile Val Leu Gly Ser Leu Leu Gly Leu Ala  
 740 745 750  
 Leu Leu Ala Val Leu Leu Leu Leu Cys Ile Cys Cys Leu Cys Arg Phe  
 755 760 765  
 Arg Gly Lys Thr Pro Glu Lys Lys Lys His Pro Ser Thr Leu Val Pro  
 770 775 780  
 Val Val Thr Pro Ser Glu Lys Lys Met His Ser Val Thr Pro Val Glu  
 785 790 795 800  
 Ile Ser Trp Pro Leu Asp Leu Lys Val Pro Leu Glu Asp His Ser Ser  
 805 810 815  
 Thr Arg Ala Tyr Gln Ala Thr Asp Pro Ser Ser Val Val Ser Val Gly  
 820 825 830  
 Gly Gly Ser Lys Thr Val Arg Ala Ala Thr Gln Val  
 835 840

&lt;210&gt; 57

&lt;211&gt; 782

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 57

Met Asp Asn Pro Gln Ala Leu Pro Leu Phe Leu Leu Leu Ala Ser Leu  
 1 5 10 15  
 Val Gly Ile Leu Thr Leu Arg Ala Ser Ser Gly Leu Gln Gln Thr Asn  
 20 25 30  
 Phe Ser Ser Ala Phe Ser Ser Asp Ser Lys Ser Ser Ser Gln Gly Leu  
 35 40 45  
 Gly Val Glu Val Pro Ser Ile Lys Pro Pro Ser Trp Lys Val Pro Asp  
 50 55 60  
 Gln Phe Leu Asp Ser Lys Ala Ser Ala Gly Ile Ser Asp Ser Ser Trp  
 65 70 75 80  
 Phe Pro Glu Ala Leu Ser Ser Asn Met Ser Gly Ser Phe Trp Ser Asn  
 85 90 95  
 Val Ser Ala Glu Gly Gln Asp Leu Ser Pro Val Ser Pro Phe Ser Glu  
 100 105 110  
 Thr Pro Gly Ser Glu Val Phe Pro Asp Ile Ser Asp Pro Gln Val Pro  
 115 120 125

Ala	Lys	Asp	Pro	Lys	Pro	Ser	Phe	Thr	Val	Lys	Thr	Pro	Ala	Ser	Asn	130	135	140
Ile	Ser	Thr	Gln	Val	Ser	His	Thr	Lys	Leu	Ser	Val	Glu	Ala	Pro	Asp	145	150	155
Ser	Lys	Phe	Ser	Pro	Asp	Asp	Met	Asp	Leu	Lys	Leu	Ser	Ala	Gln	Ser	165	170	175
Pro	Glu	Ser	Lys	Phe	Ser	Ala	Glu	Thr	His	Ser	Ala	Ala	Ser	Phe	Pro	180	185	190
Gln	Gln	Val	Gly	Gly	Pro	Leu	Ala	Val	Leu	Val	Gly	Thr	Thr	Ile	Arg	195	200	205
Leu	Pro	Leu	Val	Pro	Ile	Pro	Asn	Pro	Gly	Pro	Pro	Thr	Ser	Leu	Val	210	215	220
Val	Trp	Arg	Arg	Gly	Ser	Lys	Val	Leu	Ala	Ala	Gly	Gly	Leu	Gly	Pro	225	230	235
Gly	Ala	Pro	Leu	Ile	Ser	Leu	Asp	Pro	Ala	His	Arg	Asp	His	Leu	Arg	245	250	255
Phe	Asp	Gln	Ala	Arg	Gly	Val	Leu	Glu	Leu	Ala	Ser	Ala	Gln	Leu	Asp	260	265	270
Asp	Ala	Gly	Val	Tyr	Thr	Ala	Glu	Val	Ile	Arg	Ala	Gly	Val	Ser	Gln	275	280	285
Gln	Thr	His	Glu	Phe	Thr	Val	Gly	Val	Tyr	Glu	Pro	Leu	Pro	Gln	Leu	290	295	300
Ser	Val	Gln	Pro	Lys	Ala	Pro	Glu	Thr	Glu	Glu	Gly	Ala	Ala	Glu	Leu	305	310	315
Arg	Leu	Arg	Cys	Leu	Gly	Trp	Gly	Pro	Gly	Arg	Gly	Glu	Leu	Ser	Trp	325	330	335
Ser	Arg	Asp	Gly	Arg	Ala	Leu	Glu	Ala	Glu	Ser	Glu	Gly	Ala	Glu		340	345	350
Thr	Pro	Arg	Met	Arg	Ser	Glu	Gly	Asp	Gln	Leu	Leu	Ile	Val	Arg	Pro	355	360	365
Val	Arg	Ser	Asp	His	Ala	Arg	Tyr	Thr	Cys	Arg	Val	Arg	Ser	Pro	Phe	370	375	380
Gly	His	Arg	Glu	Ala	Ala	Ala	Asp	Val	Ser	Val	Phe	Tyr	Gly	Pro	Asp	385	390	395
Pro	Pro	Thr	Ile	Thr	Val	Ser	Ser	Asp	Arg	Asp	Ala	Ala	Pro	Ala	Arg	405	410	415
Phe	Val	Thr	Ala	Gly	Ser	Asn	Val	Thr	Leu	Arg	Cys	Ala	Ala	Ala	Ser	420	425	430
Arg	Pro	Pro	Ala	Asp	Ile	Thr	Trp	Ser	Leu	Ala	Asp	Pro	Ala	Glu	Ala	435	440	445
Ala	Val	Pro	Ala	Gly	Ser	Arg	Leu	Leu	Leu	Pro	Ala	Val	Gly	Pro	Gly	450	455	460
His	Ala	Gly	Thr	Tyr	Ala	Cys	Leu	Ala	Ala	Asn	Pro	Arg	Thr	Gly	Arg	465	470	475
Arg	Arg	Arg	Ser	Leu	Leu	Asn	Leu	Thr	Val	Ala	Asp	Leu	Pro	Pro	Gly	485	490	495
Ala	Pro	Gln	Cys	Ser	Val	Glu	Gly	Gly	Pro	Gly	Asp	Arg	Ser	Leu	Arg	500	505	510
Phe	Arg	Cys	Ser	Trp	Pro	Gly	Gly	Ala	Pro	Ala	Ala	Ser	Leu	Gln	Phe	515	520	525
Gln	Gly	Leu	Pro	Glu	Gly	Ile	Arg	Ala	Gly	Pro	Val	Ser	Ser	Val	Leu	530	535	540
Leu	Ala	Ala	Val	Pro	Ala	His	Pro	Arg	Leu	Ser	Gly	Val	Pro	Ile	Thr	545	550	555
Cys	Leu	Ala	Arg	His	Leu	Val	Ala	Thr	Arg	Thr	Cys	Thr	Val	Thr	Pro	565	570	575
Glu	Ala	Pro	Arg	Glu	Val	Leu	Leu	His	Pro	Leu	Val	Ala	Glu	Thr	Arg	580	585	590
Leu	Gly	Glu	Ala	Glu	Val	Ala	Leu	Glu	Ala	Ser	Gly	Cys	Pro	Pro	Pro			

595 600 605  
 Ser Arg Ala Ser Trp Ala Arg Glu Gly Arg Pro Leu Ala Pro Gly Gly  
 610 615 620  
 Gly Ser Arg Leu Arg Leu Ser Gln Asp Gly Arg Lys Leu His Ile Gly  
 625 630 635 640  
 Asn Phe Ser Leu Asp Trp Asp Leu Gly Asn Tyr Ser Val Leu Cys Ser  
 645 650 655  
 Gly Ala Leu Gly Ala Gly Gly Asp Gln Ile Thr Leu Ile Gly Pro Thr  
 660 665 670  
 Leu Ser His Gly Ala Ile Ala Gly Ile Val Leu Gly Ser Leu Leu Gly  
 675 680 685  
 Leu Ala Leu Leu Ala Val Leu Leu Leu Cys Ile Cys Cys Leu Cys  
 690 695 700  
 Arg Phe Arg Gly Lys Thr Pro Glu Lys Lys Lys His Pro Ser Thr Leu  
 705 710 715 720  
 Val Pro Val Val Thr Pro Ser Glu Lys Lys Met His Ser Val Thr Pro  
 725 730 735  
 Val Glu Ile Ser Trp Pro Leu Asp Leu Lys Val Pro Leu Glu Asp His  
 740 745 750  
 Ser Ser Thr Arg Ala Tyr Gln Ala Thr Asp Pro Ser Ser Val Val Ser  
 755 760 765  
 Val Gly Gly Gly Ser Lys Thr Val Arg Ala Ala Thr Gln Val  
 770 775 780

<210> 58  
 <211> 262  
 <212> PRT  
 <213> Homo sapiens

<400> 58  
 Met Asp Ser Leu Val Thr Ala Asn Thr Lys Phe Cys Phe Asp Leu Phe  
 1 5 10 15  
 Gln Glu Ile Gly Lys Asp Asp Arg His Lys Asn Ile Phe Phe Ser Pro  
 20 25 30  
 Leu Ser Leu Ser Ala Ala Leu Gly Met Val Arg Leu Gly Ala Arg Ser  
 35 40 45  
 Asp Ser Ala His Gln Ile Asp Glu Ala Gly Ser Leu Asn Asn Glu Ser  
 50 55 60  
 Gly Leu Val Ser Cys Tyr Phe Gly Gln Leu Leu Ser Lys Leu Asp Arg  
 65 70 75 80  
 Ile Lys Thr Asp Tyr Thr Leu Ser Ile Ala Asn Arg Leu Tyr Gly Glu  
 85 90 95  
 Gln Glu Phe Pro Ile Cys Gln Glu Tyr Leu Asp Gly Val Ile Gln Phe  
 100 105 110  
 Tyr His Thr Thr Ile Glu Ser Val Asp Phe Gln Lys Asn Pro Glu Lys  
 115 120 125  
 Ser Arg Gln Glu Ile Asn Phe Trp Val Glu Cys Gln Ser Gln Gly Lys  
 130 135 140  
 Ile Lys Glu Leu Phe Ser Lys Asp Ala Ile Asn Ala Glu Thr Val Leu  
 145 150 155 160  
 Val Leu Val Asn Ala Val Tyr Phe Lys Ala Lys Trp Glu Thr Tyr Phe  
 165 170 175  
 Asp His Glu Asn Thr Val Asp Ala Pro Phe Cys Leu Asn Ala Asn Glu  
 180 185 190  
 Asn Lys Ser Val Lys Met Met Thr Gln Lys Gly Leu Tyr Arg Ile Gly  
 195 200 205  
 Phe Ile Glu Glu Val Lys Ala Gln Ile Leu Glu Met Arg Tyr Thr Lys  
 210 215 220  
 Gly Lys Leu Ser Met Phe Val Leu Leu Pro Ser His Ser Lys Asp Asn

225			230			235			240						
Leu	Lys	Gly	Leu	Glu	Glu	Val	Asn	Leu	His	Phe	His	Ile	Ser	Thr	Lys
			245						250			255			
Tyr	Leu	Met	Ile	Asp	Leu										
			260												
			<210> 59												
			<211> 394												
			<212> PRT												
			<213> Homo sapiens												
			<400> 59												
Met	Asp	Ser	Leu	Val	Thr	Ala	Asn	Thr	Lys	Phe	Cys	Phe	Asp	Leu	Phe
1				5					10					15	
Gln	Glu	Ile	Gly	Lys	Asp	Asp	Arg	His	Lys	Asn	Ile	Phe	Phe	Ser	Pro
			20					25					30		
Leu	Ser	Leu	Ser	Ala	Ala	Leu	Gly	Met	Val	Arg	Leu	Gly	Ala	Arg	Ser
		35					40					45			
Asp	Ser	Ala	His	Gln	Ile	Asp	Glu	Val	Leu	His	Phe	Asn	Lys	Thr	Thr
	50					55					60				
Glu	Pro	Leu	Asp	Gln	Gln	Ala	Gly	Ser	Leu	Asn	Asn	Glu	Ser	Gly	Leu
				70						75					80
Val	Ser	Cys	Tyr	Phe	Gly	Gln	Leu	Leu	Ser	Lys	Leu	Asp	Arg	Ile	Lys
				85					90					95	
Thr	Asp	Tyr	Thr	Leu	Ser	Ile	Ala	Asn	Arg	Leu	Tyr	Gly	Glu	Gln	Glu
			100					105					110		
Phe	Pro	Ile	Cys	Gln	Glu	Tyr	Leu	Asp	Gly	Val	Ile	Gln	Phe	Tyr	His
		115					120					125			
Thr	Thr	Ile	Glu	Ser	Val	Asp	Phe	Gln	Lys	Asn	Pro	Glu	Lys	Ser	Arg
	130					135					140				
Gln	Glu	Ile	Asn	Phe	Trp	Val	Glu	Cys	Gln	Ser	Gln	Gly	Lys	Ile	Lys
				150						155					160
Glu	Leu	Phe	Ser	Lys	Asp	Ala	Ile	Asn	Ala	Glu	Thr	Val	Leu	Val	Leu
				165					170					175	
Val	Asn	Ala	Val	Tyr	Phe	Lys	Ala	Lys	Trp	Glu	Thr	Tyr	Phe	Asp	His
			180					185					190		
Glu	Asn	Thr	Val	Asp	Ala	Pro	Phe	Cys	Leu	Asn	Ala	Asn	Glu	Asn	Lys
		195				200						205			
Ser	Val	Lys	Met	Met	Thr	Gln	Lys	Gly	Leu	Tyr	Arg	Ile	Gly	Phe	Ile
	210					215					220				
Glu	Glu	Val	Lys	Ala	Gln	Ile	Leu	Glu	Met	Arg	Tyr	Thr	Lys	Gly	Lys
				230						235					240
Leu	Ser	Met	Phe	Val	Leu	Leu	Pro	Ser	His	Ser	Lys	Asp	Asn	Leu	Lys
			245						250					255	
Gly	Leu	Glu	Glu	Leu	Glu	Arg	Lys	Ile	Thr	Tyr	Glu	Lys	Met	Val	Ala
			260					265					270		
Trp	Ser	Ser	Ser	Glu	Asn	Met	Ser	Glu	Glu	Ser	Val	Val	Leu	Ser	Phe
		275				280						285			
Pro	Arg	Phe	Thr	Leu	Glu	Asp	Ser	Tyr	Asp	Leu	Asn	Ser	Ile	Leu	

370  
Ile Leu Phe Tyr Gly Arg Val Cys Ser Pro  
385 390

380

<210> 60  
<211> 471  
<212> PRT  
<213> Homo sapiens

<400> 60  
Met Ser Val Pro Leu Leu Lys Ile Gly Val Val Leu Ser Thr Met Ala  
1 5 10 15  
Met Ile Thr Asn Trp Met Ser Gln Thr Leu Pro Ser Leu Val Gly Leu  
20 25 30  
Asn Thr Thr Lys Leu Ser Ala Ala Gly Gly Gly Thr Leu Asp Arg Ser  
35 40 45  
Thr Gly Val Leu Pro Thr Asn Pro Glu Glu Ser Trp Gln Val Tyr Ser  
50 55 60  
Ser Ala Gln Asp Ser Glu Gly Arg Cys Ile Cys Thr Val Val Ala Pro  
65 70 75 80  
Gln Gln Thr Met Cys Ser Arg Asp Ala Arg Thr Lys Gln Leu Arg Gln  
85 90 95  
Leu Leu Glu Lys Val Gln Asn Met Ser Gln Ser Ile Glu Val Leu Asp  
100 105 110  
Arg Arg Thr Gln Arg Asp Leu Gln Tyr Val Glu Lys Met Glu Asn Gln  
115 120 125  
Met Lys Gly Leu Glu Ser Lys Phe Lys Gln Ala Ile Lys Ala Lys Met  
130 135 140  
Asp Glu Leu Arg Pro Leu Ile Pro Val Leu Glu Tyr Lys Ala Asp  
145 150 155 160  
Ala Lys Leu Val Leu Gln Phe Lys Glu Glu Val Gln Asn Leu Thr Ser  
165 170 175  
Val Leu Asn Glu Leu Gln Glu Glu Ile Gly Ala Tyr Asp Tyr Asp Glu  
180 185 190  
Leu Gln Ser Arg Val Ser Asn Leu Glu Glu Arg Leu Arg Ala Cys Met  
195 200 205  
Gln Lys Leu Ala Cys Gly Lys Leu Thr Gly Ile Ser Asp Pro Val Thr  
210 215 220  
Val Lys Thr Ser Gly Ser Arg Phe Gly Ser Trp Met Thr Asp Pro Leu  
225 230 235 240  
Ala Pro Glu Gly Asp Asn Arg Val Trp Tyr Met Asp Gly Tyr His Asn  
245 250 255  
Asn Arg Phe Val Arg Glu Tyr Lys Ser Met Val Asp Phe Met Asn Thr  
260 265 270  
Asp Asn Phe Thr Ser His Arg Leu Pro His Pro Trp Ser Gly Thr Gly  
275 280 285  
Gln Val Val Tyr Asn Gly Ser Ile Tyr Phe Asn Lys Phe Gln Ser His  
290 295 300  
Ile Ile Ile Arg Phe Asp Leu Lys Thr Glu Thr Ile Leu Lys Thr Arg  
305 310 315 320  
Ser Leu Asp Tyr Ala Gly Tyr Asn Asn Met Tyr His Tyr Ala Trp Gly  
325 330 335  
Gly His Ser Asp Ile Asp Leu Met Val Asp Glu Ser Gly Leu Trp Ala  
340 345 350  
Val Tyr Ala Thr Asn Gln Asn Ala Gly Asn Ile Val Val Ser Arg Leu  
355 360 365  
Asp Pro Val Ser Leu Gln Thr Leu Gln Thr Trp Asn Thr Ser Tyr Pro  
370 375 380  
Lys Arg Ser Ala Gly Glu Ala Phe Ile Ile Cys Gly Thr Leu Tyr Val

385                                      390                                      395                                      400  
 Thr Asn Gly Tyr Ser Gly Gly Thr Lys Val His Tyr Ala Tyr Gln Thr  
    405                                      410                                      415  
 Asn Ala Ser Thr Tyr Glu Tyr Ile Asp Ile Pro Phe Gln Asn Lys Tyr  
    420                                      425                                      430  
 Ser His Ile Ser Met Leu Asp Tyr Asn Pro Lys Asp Arg Ala Leu Tyr  
    435                                      440                                      445  
 Ala Trp Asn Asn Gly His Gln Ile Leu Tyr Asn Val Thr Leu Phe His  
    450                                      455                                      460  
 Val Ile Arg Ser Asp Glu Leu  
 465                                      470

<210> 61  
 <211> 485  
 <212> PRT  
 <213> Homo sapiens

<400> 61  
 Met Ser Val Pro Leu Leu Lys Ile Gly Val Val Leu Ser Thr Met Ala  
 1                                      5                                      10                                      15  
 Met Ile Thr Asn Trp Met Ser Gln Thr Leu Pro Ser Leu Val Gly Leu  
    20                                      25                                      30  
 Asn Thr Thr Lys Leu Ser Ala Ala Gly Gly Gly Thr Leu Asp Arg Ser  
    35                                      40                                      45  
 Thr Gly Val Leu Pro Thr Asn Pro Glu Glu Ser Trp Gln Val Tyr Ser  
    50                                      55                                      60  
 Ser Ala Gln Asp Ser Glu Gly Arg Cys Ile Cys Thr Val Val Ala Pro  
 65                                      70                                      75                                      80  
 Gln Gln Thr Met Cys Ser Arg Asp Ala Arg Thr Lys Gln Leu Arg Gln  
    85                                      90                                      95  
 Leu Leu Glu Lys Val Gln Asn Met Ser Gln Ser Ile Glu Val Leu Asp  
    100                                      105                                      110  
 Arg Arg Thr Gln Arg Asp Leu Gln Tyr Val Glu Lys Met Glu Asn Gln  
    115                                      120                                      125  
 Met Lys Gly Leu Glu Ser Lys Phe Lys Gln Val Glu Glu Ile Ile Ser  
    130                                      135                                      140  
 Tyr Thr Trp Pro Arg Gln Phe Lys Ala Ile Lys Ala Lys Met Asp Glu  
 145                                      150                                      155                                      160  
 Leu Arg Pro Leu Ile Pro Val Leu Glu Glu Tyr Lys Ala Asp Ala Lys  
    165                                      170                                      175  
 Leu Val Leu Gln Phe Lys Glu Glu Val Gln Asn Leu Thr Ser Val Leu  
    180                                      185                                      190  
 Asn Glu Leu Gln Glu Glu Ile Gly Ala Tyr Asp Tyr Asp Glu Leu Gln  
    195                                      200                                      205  
 Ser Arg Val Ser Asn Leu Glu Glu Arg Leu Arg Ala Cys Met Gln Lys  
    210                                      215                                      220  
 Leu Ala Cys Gly Lys Leu Thr Gly Ile Ser Asp Pro Val Thr Val Lys  
 225                                      230                                      235                                      240  
 Thr Ser Gly Ser Arg Phe Gly Ser Trp Met Thr Asp Pro Leu Ala Pro  
    245                                      250                                      255  
 Glu Gly Asp Asn Arg Val Trp Tyr Met Asp Gly Tyr His Asn Asn Arg  
    260                                      265                                      270  
 Phe Val Arg Glu Tyr Lys Ser Met Val Asp Phe Met Asn Thr Asp Asn  
    275                                      280                                      285  
 Phe Thr Ser His Arg Leu Pro His Pro Trp Ser Gly Thr Gly Gln Val  
    290                                      295                                      300  
 Val Tyr Asn Gly Ser Ile Tyr Phe Asn Lys Phe Gln Ser His Ile Ile  
 305                                      310                                      315                                      320  
 Ile Arg Phe Asp Leu Lys Thr Glu Thr Ile Leu Lys Thr Arg Ser Leu



325 330 335  
 Asp Tyr Ala Gly Tyr Asn Asn Met Tyr His Tyr Ala Trp Gly Gly His  
 340 345 350  
 Ser Asp Ile Asp Leu Met Val Asp Glu Ser Gly Leu Trp Ala Val Tyr  
 355 360 365  
 Ala Thr Asn Gln Asn Gly Asn Ile Val Val Ser Arg Leu Asp Pro  
 370 375 380  
 Val Ser Leu Gln Thr Leu Gln Thr Trp Asn Thr Ser Tyr Pro Lys Arg  
 385 390 395 400  
 Ser Ala Gly Glu Ala Phe Ile Ile Cys Gly Thr Leu Tyr Val Thr Asn  
 405 410 415  
 Gly Tyr Ser Gly Gly Thr Lys Val His Tyr Ala Tyr Gln Thr Asn Ala  
 420 425 430  
 Ser Thr Tyr Glu Tyr Ile Asp Ile Pro Phe Gln Asn Lys Tyr Ser His  
 435 440 445  
 Ile Ser Met Leu Asp Tyr Asn Pro Lys Asp Arg Ala Leu Tyr Ala Trp  
 450 455 460  
 Asn Asn Gly His Gln Ile Leu Tyr Asn Val Thr Leu Phe His Val Ile  
 465 470 475 480  
 Arg Ser Asp Glu Leu  
 485

<210> 62  
 <211> 286  
 <212> PRT  
 <213> Homo sapiens

<400> 62  
 Met Leu His Leu Leu Ala Leu Phe Leu His Cys Leu Pro Leu Ala Ser  
 1 5 10 15  
 Gly Asp Tyr Asp Ile Cys Lys Ser Trp Val Thr Thr Asp Glu Gly Pro  
 20 25 30  
 Thr Trp Glu Phe Tyr Ala Cys Gln Pro Lys Val Met Arg Leu Lys Asp  
 35 40 45  
 Tyr Val Lys Val Lys Val Glu Pro Ser Gly Ile Thr Cys Gly Asp Pro  
 50 55 60  
 Pro Glu Arg Phe Cys Ser His Glu Asn Pro Tyr Leu Cys Ser Asn Glu  
 65 70 75 80  
 Cys Asp Ala Ser Asn Pro Asp Leu Ala His Pro Pro Arg Leu Met Phe  
 85 90 95  
 Asp Lys Glu Glu Glu Gly Leu Ala Thr Tyr Trp Gln Ser Ile Thr Trp  
 100 105 110  
 Ser Arg Tyr Pro Ser Pro Leu Glu Ala Asn Ile Thr Leu Ser Trp Asn  
 115 120 125  
 Lys Thr Val Glu Leu Thr Asp Asp Val Val Met Thr Phe Glu Tyr Gly  
 130 135 140  
 Arg Pro Thr Val Met Val Leu Glu Lys Ser Leu Asp Asn Gly Arg Thr  
 145 150 155 160  
 Trp Gln Pro Tyr Gln Phe Tyr Ala Glu Asp Cys Met Glu Ala Phe Gly  
 165 170 175  
 Met Ser Ala Arg Arg Ala Arg Asp Met Ser Ser Ser Ala His Arg  
 180 185 190  
 Val Leu Cys Thr Glu Glu Tyr Ser Arg Trp Ala Gly Ser Lys Lys Glu  
 195 200 205  
 Lys His Val Arg Phe Glu Val Arg Asp Arg Phe Ala Ile Phe Ala Gly  
 210 215 220  
 Pro Asp Leu Arg Asn Met Asp Asn Leu Tyr Thr Arg Leu Glu Ser Ala  
 225 230 235 240  
 Lys Gly Leu Lys Glu Phe Phe Thr Leu Thr Asp Leu Arg Met Arg Leu

				245					250					255			
Leu	Arg	Pro	Ala	Leu	Gly	Gly	Thr	Tyr	Val	Gln	Arg	Glu	Asn	Leu	Tyr		
			260					265					270				
Lys	Tyr	Phe	Tyr	Ala	Ile	Ser	Asn	Ile	Glu	Val	Ile	Gly	Arg				
		275					280					285					

&lt;210&gt; 63

&lt;211&gt; 533

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 63

Met	Leu	His	Leu	Leu	Ala	Leu	Phe	Leu	His	Cys	Leu	Pro	Leu	Ala	Ser		
1			5					10						15			
Gly	Asp	Tyr	Asp	Ile	Cys	Lys	Ser	Trp	Val	Thr	Thr	Asp	Glu	Gly	Pro		
		20					25						30				
Thr	Trp	Glu	Phe	Tyr	Ala	Cys	Gln	Pro	Lys	Val	Met	Arg	Leu	Lys	Asp		
		35					40					45					
Tyr	Val	Lys	Val	Lys	Val	Glu	Pro	Ser	Gly	Ile	Thr	Cys	Gly	Asp	Pro		
	50					55					60						
Pro	Glu	Arg	Phe	Cys	Ser	His	Glu	Asn	Pro	Tyr	Leu	Cys	Ser	Asn	Glu		
65				70					75					80			
Cys	Asp	Ala	Ser	Asn	Pro	Asp	Leu	Ala	His	Pro	Pro	Arg	Leu	Met	Phe		
			85					90						95			
Asp	Lys	Glu	Glu	Glu	Gly	Leu	Ala	Thr	Tyr	Trp	Gln	Ser	Ile	Thr	Trp		
		100					105						110				
Ser	Arg	Tyr	Pro	Ser	Pro	Leu	Glu	Ala	Asn	Ile	Thr	Leu	Ser	Trp	Asn		
		115				120						125					
Lys	Thr	Val	Glu	Leu	Thr	Asp	Asp	Val	Val	Met	Thr	Phe	Glu	Tyr	Gly		
	130					135					140						
Arg	Pro	Thr	Val	Met	Val	Leu	Glu	Lys	Ser	Leu	Asp	Asn	Gly	Arg	Thr		
145					150					155				160			
Trp	Gln	Pro	Tyr	Gln	Phe	Tyr	Ala	Glu	Asp	Cys	Met	Glu	Ala	Phe	Gly		
			165					170						175			
Met	Ser	Ala	Arg	Arg	Ala	Arg	Asp	Met	Ser	Ser	Ser	Ser	Ala	His	Arg		
		180					185						190				
Val	Leu	Cys	Thr	Glu	Glu	Tyr	Ser	Arg	Trp	Ala	Gly	Ser	Lys	Lys	Glu		
	195					200						205					
Lys	His	Val	Arg	Phe	Glu	Val	Arg	Asp	Arg	Phe	Ala	Ile	Phe	Ala	Gly		
	210					215					220						
Pro	Asp	Leu	Arg	Asn	Met	Asp	Asn	Leu	Tyr	Thr	Arg	Leu	Glu	Ser	Ala		
225				230					235					240			
Lys	Gly	Leu	Lys	Glu	Phe	Phe	Thr	Leu	Thr	Asp	Leu	Arg	Met	Arg	Leu		
			245					250						255			
Leu	Arg	Pro	Ala	Leu	Gly	Gly	Thr	Tyr	Val	Gln	Arg	Glu	Asn	Leu	Tyr		
		260					265						270				
Lys	Tyr	Phe	Tyr	Ala	Ile	Ser	Asn	Ile	Glu	Val	Ile	Gly	Arg	Cys	Lys		
	275					280						285					
Cys	Asn	Leu	His	Ala	Asn	Leu	Cys	Ser	Met	Arg	Glu	Gly	Ser	Leu	Gln		
	290				295						300						
Cys	Glu	Cys	Glu	His	Asn	Thr	Thr	Gly	Pro	Asp	Cys	Gly	Lys	Cys	Lys		
305				310						315				320			
Lys	Asn	Phe	Arg	Thr	Arg	Ser	Trp	Arg	Ala	Gly	Ser	Tyr	Leu	Pro	Leu		
			325					330						335			
Pro	His	Gly	Ser	Pro	Asn	Ala	Cys	Thr	Pro	Pro	Ser	Pro	Arg	Glu	Leu		
		340						345					350				
Gly	Ala	Asp	Cys	Glu	Cys	Tyr	Gly	His	Ser	Asn	Arg	Cys	Ser	Tyr	Ile		
	355					360						365					
Asp	Phe	Leu	Asn	Val	Val	Thr	Cys	Val	Ser	Cys	Lys	His	Asn	Thr	Arg		

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      370      375      380
Gly Gln His Cys Gln His Cys Arg Leu Gly Tyr Tyr Arg Asn Gly Ser
385      390      395      400
Ala Glu Leu Asp Asp Glu Asn Val Cys Ile Glu Cys Asn Cys Asn Gln
      405      410      415
Ile Gly Ser Val His Asp Arg Cys Asn Glu Thr Gly Phe Cys Glu Cys
      420      425      430
Arg Glu Gly Ala Ala Gly Pro Lys Cys Asp Asp Cys Leu Pro Thr His
      435      440      445
Tyr Trp Arg Gln Gly Cys Tyr Pro Asn Val Cys Asp Asp Asp Gln Leu
      450      455      460
Leu Cys Gln Asn Gly Gly Thr Cys Leu Gln Asn Gln Arg Cys Ala Cys
465      470      475      480
Pro Arg Gly Tyr Thr Gly Val Arg Cys Glu Gln Pro Arg Cys Asp Pro
      485      490      495
Ala Asp Asp Asp Gly Gly Leu Asp Cys Asp Arg Ala Pro Gly Ala Ala
      500      505      510
Pro Arg Pro Ala Thr Leu Leu Gly Cys Leu Leu Leu Leu Gly Leu Ala
      515      520      525
Ala Arg Leu Gly Arg
530

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<210> 64
<211> 495
<212> PRT
<213> Homo sapiens

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      <400> 64
Met Phe Ala Asn Ser Pro Gly Cys Ser Asn Met Leu His Tyr Val Tyr
1      5      10      15
Cys Ala Cys Gly His Gly Leu Gln Leu Val Arg Ser Val Ser Ser Ser
      20      25      30
Val Asp Glu Gly Gly Thr Cys His Cys Met Val His Leu Pro Asn Asn
      35      40      45
Pro Ile Pro Leu Glu Gln Leu Glu Gln Leu Gln Ser Thr Ala Gln Glu
50      55      60
Leu Ile Cys Lys Tyr Glu Gln Lys Leu Ser Arg Cys Ala Arg Ala Ile
65      70      75      80
Glu Asp Lys Asp Asn Glu Val Leu Glu Met Ser His Met Leu Lys Ser
      85      90      95
Trp Asn Pro Ser Ala Leu Ala Ser Pro Tyr Glu Asn Pro Gly Phe Asn
      100      105      110
Leu Leu Cys Leu Glu Leu Glu Gly Ala Gln Glu Leu Val Thr Gln Leu
      115      120      125
Lys Ala Met Gly Gly Val Ser Val Ala Gly Asp Leu Leu His Gln Leu
130      135      140
Gln Ser Gln Val Thr Asn Ala Ser Leu Thr Leu Lys Leu Leu Ala Asp
145      150      155      160
Ser Asp Gln Cys Ser Phe Gly Ala Leu Gln Gln Glu Val Asp Val Leu
      165      170      175
Glu Ser Gln Leu Ser Glu Cys Glu Arg Glu Lys Glu Lys Glu Gly Leu
      180      185      190
Trp Thr Pro Trp Thr Thr Pro Pro Ala Ser Cys Ala His Gly Gly
195      200      205
Leu Gln Glu Val Ser Lys Ser Leu Val Val Gln Leu Thr Arg Arg Gly
210      215      220
Phe Ser Tyr Lys Ala Gly Pro Trp Gly Arg Asp Ser Ala Pro Asn Pro
225      230      235      240
Ala Ser Ser Leu Tyr Trp Val Ala Pro Leu Arg Thr Asp Gly Arg Tyr

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				245					250				255				
Phe	Asp	Tyr	Tyr	Arg	Leu	Pro	Pro	Ser	Tyr	Asn	Asp	Leu	Ala	Leu	Met		
			260					265					270				
Lys	Asn	Tyr	Glu	Glu	Arg	Lys	Met	Gly	Tyr	Gly	Asp	Gly	Ser	Gly	Asn		
		275					280					285					
Val	Val	Tyr	Lys	Asn	Phe	Met	Tyr	Phe	Asn	Tyr	Cys	Gly	Thr	Ser	Asp		
	290					295					300						
Met	Ala	Lys	Met	Asp	Leu	Ser	Ser	Asn	Thr	Leu	Val	Leu	Trp	Arg	Leu		
305					310					315					320		
Leu	Pro	Gly	Ala	Thr	Tyr	Asn	Asn	Arg	Phe	Ser	Cys	Ala	Gly	Val	Pro		
				325					330					335			
Trp	Lys	Asp	Leu	Asp	Phe	Ala	Gly	Asp	Glu	Lys	Gly	Leu	Trp	Val	Leu		
		340					345						350				
Tyr	Ala	Thr	Glu	Glu	Ser	Lys	Gly	Asn	Leu	Val	Val	Ser	Arg	Leu	Asn		
	355						360					365					
Ala	Ser	Thr	Leu	Glu	Val	Glu	Lys	Thr	Trp	Arg	Thr	Ser	Gln	Tyr	Lys		
	370					375					380						
Pro	Ala	Leu	Ser	Gly	Ala	Phe	Met	Ala	Cys	Gly	Val	Leu	Tyr	Ala	Leu		
385					390				395					400			
His	Ser	Leu	Asn	Thr	His	Gln	Glu	Glu	Ile	Phe	Tyr	Ala	Phe	Asp	Thr		
			405						410					415			
Thr	Thr	Gly	Gln	Glu	Arg	Arg	Leu	Ser	Ile	Leu	Leu	Asp	Lys	Met	Leu		
		420					425						430				
Glu	Lys	Leu	Gln	Gly	Ile	Asn	Tyr	Cys	Pro	Ser	Asp	His	Lys	Pro	Tyr		
	435					440					445						
Val	Phe	Ser	Asp	Gly	Tyr	Leu	Ile	Asn	Tyr	Asp	Leu	Thr	Phe	Leu	Thr		
	450					455				460							
Met	Lys	Thr	Arg	Leu	Pro	Arg	Pro	Pro	Thr	Arg	Arg	Pro	Ser	Gly	Ala		
465					470				475					480			
His	Ala	Pro	Pro	Lys	Pro	Val	Lys	Pro	Asn	Glu	Ala	Ser	Arg	Pro			
			485					490					495				

&lt;210&gt; 65

&lt;211&gt; 350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

Met	Arg	Asn	His	Lys	Lys	Val	Thr	Asn	Ala	Ser	Leu	Thr	Leu	Lys	Leu		
1				5				10					15				
Leu	Ala	Asp	Ser	Asp	Gln	Cys	Ser	Phe	Gly	Ala	Leu	Gln	Gln	Glu	Val		
		20					25					30					
Asp	Val	Leu	Glu	Ser	Gln	Leu	Ser	Glu	Ser	Ser	Cys	Ala	His	Gly	Gly		
	35					40					45						
Leu	Gln	Glu	Val	Ser	Lys	Ser	Leu	Val	Val	Gln	Leu	Thr	Arg	Arg	Gly		
	50				55					60							
Phe	Ser	Tyr	Lys	Ala	Gly	Pro	Trp	Gly	Arg	Asp	Ser	Ala	Pro	Asn	Pro		
65				70				75						80			
Ala	Ser	Ser	Leu	Tyr	Trp	Val	Ala	Pro	Leu	Arg	Thr	Asp	Gly	Ser	Tyr		
			85				90					95					
Gly	Cys	His	Pro	Ile	Ile	Leu	Asn	Ala	Gly	Thr	Trp	Pro	Arg	Tyr	Phe		
	100					105					110						
Asp	Tyr	Tyr	Arg	Leu	Cys	Lys	Ser	Tyr	Asn	Asp	Leu	Ala	Leu	Leu	Lys		
	115					120					125						
Asn	Tyr	Glu	Glu	Arg	Lys	Met	Gly	Tyr	Gly	Asp	Gly	Ser	Gly	Asn	Val		
	130				135					140							
Val	Tyr	Lys	Asn	Phe	Met	Tyr	Phe	Asn	Tyr	Cys	Gly	Thr	Ser	Asp	Met		
145				150				155						160			
Ala	Lys	Met	Asp	Leu	Ser	Ser	Asn	Thr	Leu	Val	Leu	Trp	Arg	Leu	Leu		

				165					170					175					
Pro	Gly	Ala	Thr	Tyr	Asn	Asn	Arg	Phe	Ser	Cys	Ala	Gly	Val	Pro	Trp				
			180					185					190						
Lys	Asp	Leu	Asp	Phe	Ala	Gly	Asp	Glu	Lys	Gly	Leu	Trp	Val	Leu	Tyr				
		195					200					205							
Ala	Thr	Glu	Glu	Ser	Lys	Gly	Asn	Leu	Val	Val	Ser	Arg	Leu	Asn	Ala				
	210					215					220								
Ser	Thr	Leu	Glu	Val	Glu	Lys	Thr	Trp	Arg	Thr	Ser	Gln	Tyr	Lys	Pro				
225					230					235					240				
Ala	Leu	Ser	Gly	Ala	Phe	Met	Ala	Cys	Gly	Val	Leu	Tyr	Ala	Leu	His				
				245					250					255					
Ser	Leu	Asn	Thr	His	Gln	Glu	Glu	Ile	Phe	Tyr	Ala	Phe	Asp	Thr	Thr				
			260					265					270						
Thr	Gly	Gln	Glu	Arg	Arg	Leu	Ser	Ile	Leu	Leu	Asp	Lys	Met	Leu	Glu				
		275					280					285							
Lys	Leu	Gln	Gly	Ile	Asn	Tyr	Cys	Pro	Ser	Asp	His	Lys	Pro	Tyr	Val				
	290					295					300								
Phe	Ser	Asp	Gly	Tyr	Leu	Ile	Asn	Tyr	Asp	Leu	Thr	Phe	Leu	Thr	Met				
305					310					315					320				
Lys	Thr	Arg	Leu	Pro	Arg	Pro	Pro	Thr	Arg	Arg	Pro	Ser	Gly	Ala	His				
				325					330					335					
Ala	Pro	Pro	Lys	Pro	Val	Lys	Pro	Asn	Glu	Ala	Ser	Arg	Pro						
			340					345					350						

<210> 66  
 <211> 619  
 <212> PRT  
 <213> Homo sapiens

Met	Gly	Arg	Gly	Arg	Ala	Leu	Leu	Pro	Ile	Glu	Met	Leu	Gln	Leu	Ser				
1				5					10				15						
Leu	Arg	Glu	Glu	Ser	Asp	Thr	Ala	Arg	Met	Gly	Ala	Gln	Glu	Gln	Ile				
			20					25					30						
Gly	Leu	Gln	Asp	Glu	Ile	Gln	Ala	Ala	Asn	Ala	Gly	Ile	Ser	Gly	Ser				
		35				40						45							
Pro	Gly	Val	Asp	Gly	Val	Val	Asp	Gly	Gly	Ser	Ser	Arg	Gly	Asp	Pro				
	50					55				60									
Ala	Leu	Thr	Val	Ser	Val	Cys	Glu	Val	Pro	Pro	Val	Arg	Ser	Pro	Phe				
65					70				75						80				
Arg	Thr	His	Pro	Gln	Leu	Pro	Val	Arg	Leu	Pro	Arg	Asn	Leu	Glu	Phe				
			85					90					95						
Ser	Val	Pro	Glu	Arg	Arg	Thr	Leu	Arg	Asn	Arg	Leu	Thr	Ser	Ala	Thr				
		100						105					110						
Leu	Ala	Pro	Pro	Thr	Arg	His	Met	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Pro				
		115					120					125							
Pro	Leu	Leu	Cys	Gly	Arg	Val	Gly	Ala	Lys	Glu	Gln	Lys	Asp	Tyr	Leu				
	130					135					140								
Leu	Thr	Met	Gln	Lys	Ser	Val	Thr	Val	Gln	Glu	Gly	Leu	Cys	Val	Ser				
145					150				155						160				
Val	Leu	Cys	Ser	Phe	Ser	Tyr	Pro	Gln	Asn	Gly	Trp	Thr	Ala	Ser	Asp				
			165					170						175					
Pro	Val	His	Gly	Tyr	Trp	Phe	Arg	Ala	Gly	Asp	His	Val	Ser	Arg	Asn				
		180						185					190						
Ile	Pro	Val	Ala	Thr	Asn	Asn	Pro	Ala	Arg	Ala	Val	Gln	Glu	Glu	Thr				
	195					200						205							
Arg	Asp	Arg	Phe	His	Leu	Leu	Gly	Asp	Pro	Gln	Asn	Lys	Asp	Cys	Thr				
	210					215					220								
Leu	Ser	Ile	Arg	Asp	Thr	Arg	Glu	Ser	Asp	Ala	Gly	Thr	Tyr	Val	Phe				

225					230					235					240
Cys	Val	Glu	Arg	Gly	Asn	Met	Lys	Trp	Asn	Tyr	Lys	Tyr	Asp	Gln	Leu
				245					250					255	
Ser	Val	Asn	Val	Thr	Ala	Leu	Thr	His	Met	Pro	Thr	Phe	Ser	Ile	Pro
			260					265					270		
Gly	Thr	Leu	Glu	Ser	Gly	His	Pro	Arg	Asn	Leu	Thr	Cys	Ser	Val	Pro
		275					280					285			
Trp	Ala	Cys	Glu	Gln	Gly	Thr	Pro	Pro	Thr	Ile	Thr	Trp	Met	Gly	Ala
	290					295					300				
Ser	Val	Ser	Ser	Leu	Asp	Pro	Thr	Ile	Thr	Arg	Ser	Ser	Met	Leu	Ser
305					310					315					320
Leu	Ile	Pro	Gln	Pro	Gln	Asp	His	Gly	Thr	Ser	Leu	Thr	Cys	Gln	Val
			325					330						335	
Thr	Leu	Pro	Gly	Ala	Gly	Val	Thr	Met	Thr	Arg	Ala	Val	Arg	Leu	Asn
			340					345					350		
Ile	Ser	Tyr	Pro	Pro	Gln	Asn	Leu	Thr	Met	Thr	Val	Phe	Gln	Gly	Asp
		355					360					365			
Gly	Thr	Ala	Ser	Thr	Thr	Leu	Arg	Asn	Gly	Ser	Ala	Leu	Ser	Val	Leu
	370					375					380				
Glu	Gly	Gln	Ser	Leu	His	Leu	Val	Cys	Ala	Val	Asp	Ser	Asn	Pro	Pro
385					390					395					400
Ala	Arg	Leu	Ser	Trp	Thr	Trp	Gly	Ser	Leu	Thr	Leu	Ser	Pro	Ser	Gln
			405						410					415	
Ser	Ser	Asn	Leu	Gly	Val	Leu	Glu	Leu	Pro	Arg	Val	His	Val	Lys	Asp
		420						425					430		
Glu	Gly	Glu	Phe	Thr	Cys	Arg	Ala	Gln	Asn	Pro	Leu	Gly	Ser	Gln	His
		435					440					445			
Ile	Ser	Leu	Ser	Leu	Ser	Leu	Gln	Asn	Glu	Tyr	Thr	Gly	Lys	Met	Arg
	450					455					460				
Pro	Ile	Ser	Gly	Val	Thr	Leu	Gly	Ala	Phe	Gly	Gly	Ala	Gly	Ala	Thr
465					470					475					480
Ala	Leu	Val	Phe	Leu	Tyr	Phe	Cys	Ile	Ile	Phe	Val	Val	Val	Arg	Ser
			485						490					495	
Cys	Arg	Lys	Lys	Ser	Ala	Arg	Pro	Ala	Val	Gly	Val	Gly	Asp	Thr	Gly
		500						505					510		
Met	Glu	Asp	Ala	Asn	Ala	Val	Arg	Gly	Ser	Ala	Ser	Gln	Met	Glu	Glu
		515						520					525		
Gly	Thr	Pro	Gly	Pro	Pro	Ser	Trp	Met	Leu	Ser	Gly	Ala	Cys	Trp	Pro
	530					535					540				
His	Cys	Ser	Ala	Leu	Thr	Pro	Phe	Ser	Ser	Ser	Ile	Gln	Gly	Pro	Leu
545					550					555					560
Ile	Glu	Ser	Pro	Ala	Asp	Asp	Ser	Pro	Pro	His	His	Ala	Pro	Pro	Ala
			565						570					575	
Leu	Ala	Thr	Pro	Ser	Pro	Glu	Glu	Gly	Glu	Ile	Gln	Tyr	Ala	Ser	Leu
		580						585					590		
Ser	Phe	His	Lys	Ala	Arg	Pro	Gln	Tyr	Pro	Gln	Glu	Gln	Glu	Ala	Ile
		595					600					605			
Gly	Tyr	Glu	Tyr	Ser	Glu	Ile	Asn	Ile	Pro	Lys					
	610					615									

&lt;210&gt; 67

&lt;211&gt; 490

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 67

Met	Leu	Leu	Leu	Leu	Leu	Leu	Pro	Pro	Leu	Leu	Cys	Gly	Arg	Val	
1				5				10					15		
Gly	Ala	Lys	Glu	Gln	Lys	Asp	Tyr	Leu	Leu	Thr	Met	Gln	Lys	Ser	Val

			20					25					30				
Thr	Val	Gln	Glu	Gly	Leu	Cys	Val	Ser	Val	Leu	Cys	Ser	Phe	Ser	Tyr		
		35					40					45					
Pro	Gln	Asn	Gly	Trp	Thr	Ala	Ser	Asp	Pro	Val	His	Gly	Tyr	Trp	Phe		
	50					55					60						
Arg	Ala	Gly	Asp	His	Val	Ser	Arg	Asn	Ile	Pro	Val	Ala	Thr	Asn	Asn		
65					70					75					80		
Pro	Ala	Arg	Ala	Val	Gln	Glu	Glu	Thr	Arg	Asp	Arg	Phe	His	Leu	Leu		
			85					90						95			
Gly	Asp	Pro	Gln	Asn	Lys	Asp	Cys	Thr	Leu	Ser	Ile	Arg	Asp	Thr	Arg		
		100						105					110				
Glu	Ser	Asp	Ala	Gly	Thr	Tyr	Val	Phe	Cys	Val	Glu	Arg	Gly	Asn	Met		
	115						120					125					
Lys	Trp	Asn	Tyr	Lys	Tyr	Asp	Gln	Leu	Ser	Val	Asn	Val	Thr	Ala	Leu		
	130					135					140						
Thr	His	Met	Pro	Thr	Phe	Ser	Ile	Pro	Gly	Thr	Leu	Glu	Ser	Gly	His		
145					150					155					160		
Pro	Arg	Asn	Leu	Thr	Cys	Ser	Val	Pro	Trp	Ala	Cys	Glu	Gln	Gly	Thr		
			165					170						175			
Pro	Pro	Thr	Ile	Thr	Trp	Met	Gly	Ala	Ser	Val	Ser	Ser	Leu	Asp	Pro		
			180					185					190				
Thr	Ile	Thr	Arg	Ser	Ser	Met	Leu	Ser	Leu	Ile	Pro	Gln	Pro	Gln	Asp		
	195						200					205					
His	Gly	Thr	Ser	Leu	Thr	Cys	Gln	Val	Thr	Leu	Pro	Gly	Ala	Gly	Val		
	210					215					220						
Thr	Met	Thr	Arg	Ala	Val	Arg	Leu	Asn	Ile	Ser	Tyr	Pro	Pro	Gln	Asn		
225					230					235					240		
Leu	Thr	Met	Thr	Val	Phe	Gln	Gly	Asp	Gly	Thr	Ala	Ser	Thr	Thr	Leu		
			245					250						255			
Arg	Asn	Gly	Ser	Ala	Leu	Ser	Val	Leu	Glu	Gly	Gln	Ser	Leu	His	Leu		
		260						265					270				
Val	Cys	Ala	Val	Asp	Ser	Asn	Pro	Pro	Ala	Arg	Leu	Ser	Trp	Thr	Trp		
	275						280					285					
Gly	Ser	Leu	Thr	Leu	Ser	Pro	Ser	Gln	Ser	Ser	Asn	Leu	Gly	Val	Leu		
	290					295					300						
Glu	Leu	Pro	Arg	Val	His	Val	Lys	Asp	Glu	Gly	Glu	Phe	Thr	Cys	Arg		
305					310					315					320		
Ala	Gln	Asn	Pro	Leu	Gly	Ser	Gln	His	Ile	Ser	Leu	Ser	Leu	Ser	Leu		
			325					330						335			
Gln	Asn	Glu	Tyr	Thr	Gly	Lys	Met	Arg	Pro	Ile	Ser	Gly	Val	Thr	Leu		
		340						345					350				
Gly	Ala	Phe	Gly	Gly	Ala	Gly	Ala	Thr	Ala	Leu	Val	Phe	Leu	Tyr	Phe		
	355						360					365					
Cys	Ile	Phe	Val	Val	Val	Arg	Ser	Cys	Arg	Lys	Lys	Ser	Ala	Arg			
	370					375				380							
Pro	Ala	Val	Gly	Val	Gly	Asp	Thr	Gly	Met	Glu	Asp	Ala	Asn	Ala	Val		
385					390					395					400		
Arg	Gly	Ser	Ala	Ser	Gln	Gly	Pro	Leu	Thr	Glu	Ser	Trp	Lys	Asp	Gly		
			405					410						415			
Asn	Pro	Leu	Lys	Lys	Pro	Pro	Pro	Ala	Val	Ala	Pro	Ser	Ser	Gly	Glu		
		420						425					430				
Glu	Gly	Glu	Leu	His	Tyr	Ala	Thr	Leu	Ser	Phe	His	Lys	Val	Lys	Pro		
	435						440					445					
Gln	Asp	Pro	Gln	Gly	Gln	Glu	Ala	Thr	Asp	Ser	Glu	Tyr	Ser	Glu	Ile		
	450					455					460						
Lys	Ile	His	Lys	Arg	Glu	Thr	Ala	Glu	Thr	Gln	Ala	Cys	Leu	Arg	Asn		
465					470					475					480		
His	Asn	Pro	Ser	Ser	Lys	Glu	Val	Arg	Gly								
				485					490								

<210> 68  
 <211> 462  
 <212> PRT  
 <213> Homo sapiens

<400> 68  
 Met Leu Pro Leu Trp Thr Leu Ser Leu Leu Leu Gly Ala Val Ala Gly  
 1 5 10 15  
 Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Ser Asp Asp Ser Pro  
 20 25 30  
 Trp Ser Gly Ile Thr Glu Arg Pro Leu His Ile Leu Pro Trp Ser Pro  
 35 40 45  
 Lys Asp Val Asn Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro Asn  
 50 55 60  
 Asn Phe Gln Glu Ile Ser Ala Val Asn Ser Ser Thr Ile Gln Ala Ser  
 65 70 75 80  
 Tyr Phe Gly Thr Asp Lys Ile Thr Arg Ile Asn Ile Ala Gly Trp Lys  
 85 90 95  
 Thr Asp Gly Lys Trp Gln Arg Asp Met Cys Asn Val Leu Leu Gln Leu  
 100 105 110  
 Glu Asp Ile Asn Cys Ile Asn Leu Asp Trp Ile Asn Gly Ser Arg Glu  
 115 120 125  
 Tyr Ile His Ala Val Asn Asn Leu Arg Val Val Gly Ala Glu Val Ala  
 130 135 140  
 Tyr Phe Ile Asp Val Leu Met Lys Lys Phe Glu Tyr Ser Pro Ser Lys  
 145 150 155 160  
 Val His Leu Ile Gly His Ser Leu Gly Ala His Leu Ala Gly Glu Ala  
 165 170 175  
 Gly Ser Arg Ile Pro Gly Leu Gly Arg Ile Thr Gly Lys His Ala Leu  
 180 185 190  
 Gln Leu Gly Leu Glu Cys Ala Thr Glu Gly Tyr Leu Leu Ser Ala Thr  
 195 200 205  
 Leu Ala Asn Asn Val Asn Phe Val Asp Thr Asn His Met Asp Ala Thr  
 210 215 220  
 Pro Ile Ile Pro Gln Trp Met Arg Gly Thr Ser Gly Thr Ser Asn Pro  
 225 230 235 240  
 Leu Pro Val Thr Ser Ser Leu Cys Leu Trp Leu Ala Asp Leu Gly Ser  
 245 250 255  
 Val Ser Leu Val Cys Leu Trp Pro Glu Met Ala Ser Phe Phe Asp Cys  
 260 265 270  
 Asn His Ala Arg Ser Tyr Gln Phe Tyr Ala Glu Ser Ile Leu Asn Pro  
 275 280 285  
 Asp Ala Phe Ile Ala Tyr Pro Cys Arg Ser Tyr Thr Ser Phe Lys Ala  
 290 295 300  
 Gly Asn Cys Phe Phe Cys Ser Lys Glu Gly Cys Pro Thr Met Gly His  
 305 310 315 320  
 Phe Ala Asp Arg Phe His Phe Lys Asn Met Lys Thr Asn Gly Ser His  
 325 330 335  
 Tyr Phe Leu Asn Thr Gly Ser Leu Ser Pro Phe Ala Arg Trp Arg His  
 340 345 350  
 Lys Leu Ser Val Lys Leu Ser Gly Ser Glu Val Thr Gln Gly Thr Val  
 355 360 365  
 Phe Leu Arg Val Gly Gly Ala Val Arg Lys Thr Gly Glu Phe Ala Ile  
 370 375 380  
 Val Ser Gly Lys Leu Glu Pro Gly Met Thr Tyr Thr Lys Leu Ile Asp  
 385 390 395 400  
 Ala Asp Val Asn Val Gly Asn Ile Thr Ser Val Gln Phe Ile Trp Lys  
 405 410 415



Lys His Leu Phe Glu Asp Ser Gln Asn Lys Leu Gly Ala Glu Met Val  
 420 425 430  
 Ile Asn Thr Ser Gly Lys Tyr Gly Tyr Lys Ser Thr Phe Cys Ser Gln  
 435 440 445  
 Asp Ile Met Gly Pro Asn Ile Leu Gln Asn Leu Lys Pro Cys  
 450 455 460

<210> 69  
 <211> 255  
 <212> PRT  
 <213> Homo sapiens

<400> 69  
 Met Val Leu Leu Val Ile Leu Ile Pro Val Leu Val Ser Ser Ala  
 1 5 10 15  
 Gly Thr Ser Ala His Tyr Glu Met Leu Gly Thr Cys Arg Met Val Cys  
 20 25 30  
 Asp Pro Tyr Gly Gly Thr Lys Ala Pro Ser Thr Ala Ala Thr Pro Asp  
 35 40 45  
 Arg Gly Leu Met Gln Ser Leu Pro Thr Phe Ile Gln Gly Pro Lys Gly  
 50 55 60  
 Glu Ala Gly Arg Pro Gly Lys Ala Gly Pro Arg Gly Pro Pro Gly Glu  
 65 70 75 80  
 Pro Gly Pro Pro Gly Pro Met Gly Pro Pro Gly Glu Lys Gly Glu Pro  
 85 90 95  
 Gly Arg Gln Gly Leu Pro Gly Pro Pro Gly Ala Pro Gly Leu Asn Ala  
 100 105 110  
 Ala Gly Ala Ile Ser Ala Ala Thr Tyr Ser Thr Gly Pro Lys Ile Ala  
 115 120 125  
 Phe Tyr Ala Gly Leu Lys Arg Gln His Glu Gly Tyr Glu Val Leu Lys  
 130 135 140  
 Phe Asp Asp Val Val Thr Asn Leu Gly Asn His Tyr Asp Pro Thr Thr  
 145 150 155 160  
 Gly Lys Phe Thr Cys Ser Ile Pro Gly Ile Tyr Phe Phe Thr Tyr His  
 165 170 175  
 Val Leu Met Arg Gly Gly Asp Gly Thr Ser Met Trp Ala Asp Leu Cys  
 180 185 190  
 Lys Asn Asn Gln Val Arg Ala Ser Ala Ile Ala Gln Asp Ala Asp Gln  
 195 200 205  
 Asn Tyr Asp Tyr Ala Ser Asn Ser Val Val Leu His Leu Glu Pro Gly  
 210 215 220  
 Asp Glu Val Tyr Ile Lys Leu Asp Gly Gly Lys Ala His Gly Gly Asn  
 225 230 235 240  
 Asn Asn Lys Tyr Ser Thr Phe Ser Gly Phe Ile Ile Tyr Ala Asp  
 245 250 255

<210> 70  
 <211> 784  
 <212> PRT  
 <213> Homo sapiens

<400> 70  
 Met Glu Gly Asp Gly Gly Thr Pro Trp Ala Leu Ala Leu Leu Arg Thr  
 1 5 10 15  
 Phe Asp Ala Gly Glu Phe Thr Gly Trp Glu Lys Val Gly Ser Gly Gly  
 20 25 30  
 Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp Leu  
 35 40 45  
 Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg Met

50						55						60					
Glu	Leu	Leu	Glu	Glu	Ala	Lys	Lys	Met	Glu	Met	Ala	Lys	Phe	Arg	Tyr		
65					70					75					80		
Ile	Leu	Pro	Val	Tyr	Gly	Ile	Cys	Arg	Glu	Pro	Val	Gly	Leu	Val	Met		
				85					90					95			
Glu	Tyr	Met	Glu	Thr	Gly	Ser	Leu	Glu	Lys	Leu	Leu	Ala	Ser	Glu	Pro		
			100					105					110				
Leu	Pro	Trp	Asp	Leu	Arg	Phe	Arg	Ile	Ile	His	Glu	Thr	Ala	Val	Gly		
			115				120					125					
Met	Asn	Phe	Leu	His	Cys	Met	Ala	Pro	Pro	Leu	Leu	His	Leu	Asp	Leu		
	130					135				140							
Lys	Pro	Ala	Asn	Ile	Leu	Leu	Asp	Ala	His	Tyr	His	Val	Lys	Ile	Ser		
145				150						155				160			
Asp	Phe	Gly	Leu	Ala	Lys	Cys	Asn	Gly	Leu	Ser	His	Ser	His	Asp	Leu		
				165				170						175			
Ser	Met	Asp	Gly	Leu	Phe	Gly	Thr	Ile	Ala	Tyr	Leu	Pro	Pro	Glu	Arg		
			180				185						190				
Ile	Arg	Glu	Lys	Ser	Arg	Leu	Phe	Asp	Thr	Lys	His	Asp	Val	Tyr	Ser		
		195				200						205					
Phe	Ala	Ile	Val	Ile	Trp	Gly	Val	Leu	Thr	Gln	Lys	Lys	Pro	Phe	Ala		
	210					215					220						
Asp	Glu	Lys	Asn	Ile	Leu	His	Ile	Met	Val	Lys	Val	Val	Lys	Gly	His		
225				230						235				240			
Arg	Pro	Glu	Leu	Pro	Pro	Val	Cys	Arg	Ala	Arg	Pro	Arg	Ala	Cys	Ser		
				245					250					255			
His	Leu	Ile	Arg	Leu	Met	Gln	Arg	Cys	Trp	Gln	Gly	Asp	Pro	Arg	Val		
			260				265						270				
Arg	Pro	Thr	Phe	Gln	Glu	Ile	Thr	Ser	Glu	Thr	Glu	Asp	Leu	Cys	Glu		
		275					280					285					
Lys	Pro	Asp	Asp	Glu	Val	Lys	Glu	Thr	Ala	His	Asp	Leu	Asp	Val	Lys		
	290					295					300						
Ser	Pro	Pro	Glu	Pro	Arg	Ser	Glu	Val	Val	Pro	Ala	Arg	Leu	Lys	Arg		
305					310					315				320			
Ala	Ser	Ala	Pro	Thr	Phe	Asp	Asn	Asp	Tyr	Ser	Leu	Ser	Glu	Leu	Leu		
				325					330					335			
Ser	Gln	Leu	Asp	Ser	Gly	Val	Ser	Gln	Ala	Val	Glu	Gly	Pro	Glu	Glu		
			340					345					350				
Leu	Ser	Arg	Ser	Ser	Ser	Glu	Ser	Lys	Leu	Pro	Ser	Ser	Gly	Ser	Gly		
		355					360					365					
Lys	Arg	Leu	Ser	Gly	Val	Ser	Ser	Val	Asp	Ser	Ala	Phe	Ser	Ser	Arg		
	370					375					380						
Gly	Ser	Leu	Ser	Leu	Ser	Phe	Glu	Arg	Glu	Pro	Ser	Thr	Ser	Asp	Leu		
385					390					395				400			
Gly	Thr	Thr	Asp	Val	Gln	Lys	Lys	Lys	Leu	Val	Asp	Ala	Ile	Val	Ser		
				405					410					415			
Gly	Asp	Thr	Ser	Lys	Leu	Met	Lys	Ile	Leu	Gln	Pro	Gln	Asp	Val	Asp		
			420					425					430				
Leu	Ala	Leu	Asp	Ser	Gly	Ala	Ser	Leu	Leu	His	Leu	Ala	Val	Glu	Ala		
		435					440					445					
Gly	Gln	Glu	Glu	Cys	Ala	Lys	Trp	Leu	Leu	Leu	Asn	Asn	Ala	Asn	Pro		
	450					455					460						
Asn	Leu	Ser	Asn	Arg	Arg	Gly	Ser	Thr	Pro	Leu	His	Met	Ala	Val	Glu		
465				470						475				480			
Arg	Arg	Val	Arg	Gly	Val	Val	Glu	Leu	Leu	Ala	Arg	Lys	Ile	Ser			
				485					490				495				
Val	Asn	Ala	Lys	Asp	Glu	Asp	Gln	Trp	Thr	Ala	Leu	His	Phe	Ala	Ala		
			500					505					510				
Gln	Asn	Gly	Asp	Glu	Ser	Ser	Thr	Arg	Leu	Leu	Leu	Glu	Lys	Asn	Ala		
		515					520					525					

Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met His Val Ala  
 530 535 540  
 Cys Gln His Gly Gln Glu Asn Ile Val Arg Ile Leu Leu Arg Arg Gly  
 545 550 555 560  
 Val Asp Val Ser Leu Gln Gly Lys Asp Ala Trp Leu Pro Leu His Tyr  
 565 570 575  
 Ala Ala Trp Gln Gly His Leu Pro Ile Val Lys Leu Leu Ala Lys Gln  
 580 585 590  
 Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg Thr Pro Leu  
 595 600 605  
 His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg Ile Leu Ile  
 610 615 620  
 Asp Leu Cys Ser Asp Val Asn Val Cys Ser Leu Leu Ala Gln Thr Pro  
 625 630 635 640  
 Leu His Val Ala Ala Glu Thr Gly His Thr Ser Thr Ala Arg Leu Leu  
 645 650 655  
 Leu His Arg Gly Ala Gly Lys Glu Ala Met Thr Ser Asp Gly Tyr Thr  
 660 665 670  
 Ala Leu His Leu Ala Ala Arg Asn Gly His Leu Ala Thr Val Lys Leu  
 675 680 685  
 Leu Val Glu Glu Lys Ala Asp Val Leu Ala Arg Gly Pro Leu Asn Gln  
 690 695 700  
 Thr Ala Leu His Leu Ala Ala His Gly His Ser Glu Val Val Glu  
 705 710 715 720  
 Glu Leu Val Ser Ala Asp Val Ile Asp Leu Phe Asp Glu Gln Gly Leu  
 725 730 735  
 Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ala Gln Thr Val Glu  
 740 745 750  
 Thr Leu Leu Arg His Gly Ala His Ile Asn Leu Gln Ser Leu Lys Phe  
 755 760 765  
 Gln Gly Gly His Gly Pro Ala Ala Thr Leu Leu Arg Arg Ser Lys Thr  
 770 775 780

<210> 71  
 <211> 252  
 <212> PRT  
 <213> Homo sapiens

<400> 71  
 Met Ala Ala Pro Ala Leu Leu Leu Leu Ala Leu Leu Leu Pro Val Gly  
 1 5 10 15  
 Ala Trp Pro Gly Leu Pro Arg Arg Pro Cys Val His Cys Cys Arg Pro  
 20 25 30  
 Ala Trp Pro Pro Gly Pro Tyr Ala Arg Val Ser Asp Arg Asp Leu Trp  
 35 40 45  
 Arg Gly Asp Leu Trp Arg Gly Leu Pro Arg Val Arg Pro Thr Ile Asp  
 50 55 60  
 Ile Glu Ile Leu Lys Gly Glu Lys Gly Glu Ala Gly Val Arg Gly Arg  
 65 70 75 80  
 Ala Gly Arg Ser Gly Lys Glu Gly Pro Pro Gly Ala Arg Gly Leu Gln  
 85 90 95  
 Gly Arg Arg Gly Gln Lys Gly Gln Val Gly Pro Pro Gly Ala Ala Cys  
 100 105 110  
 Arg Arg Ala Tyr Ala Ala Phe Ser Val Gly Arg Arg Glu Gly Leu His  
 115 120 125  
 Ser Ser Asp His Phe Gln Ala Val Pro Phe Asp Thr Glu Leu Val Asn  
 130 135 140  
 Leu Asp Gly Ala Phe Asp Leu Ala Ala Gly Arg Phe Leu Cys Thr Val  
 145 150 155 160

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Pro Gly Val Tyr Phe Leu Ser Leu Asn Val His Thr Trp Asn Tyr Lys
                165                170                175
Glu Thr Tyr Leu His Ile Met Leu Asn Arg Arg Pro Ala Ala Val Leu
                180                185                190
Tyr Ala Gln Pro Ser Glu Arg Ser Val Met Gln Ala Gln Ser Leu Met
                195                200                205
Leu Leu Leu Ala Ala Gly Asp Ala Val Trp Val Arg Met Phe Gln Arg
                210                215                220
Asp Arg Asp Asn Ala Ile Tyr Gly Glu His Gly Asp Leu Tyr Ile Thr
225                230                235                240
Phe Ser Gly His Leu Val Lys Pro Ala Ala Glu Leu
                245                250

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<210> 72
<211> 593
<212> PRT
<213> Homo sapiens

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<400> 72
Met Pro Ser Ser Leu Phe Ala Asp Leu Glu Arg Asn Gly Ser Gly Gly
 1          5          10          15
Gly Gly Gly Gly Ser Ser Gly Gly Gly Glu Thr Leu Asp Asp Gln Arg
          20          25          30
Ala Leu Gln Leu Ala Leu Asp Gln Leu Ser Leu Leu Gly Leu Asp Ser
          35          40          45
Asp Glu Gly Ala Ser Leu Tyr Asp Ser Glu Pro Arg Lys Lys Ser Val
50          55          60
Asn Met Thr Glu Cys Val Pro Val Pro Ser Ser Glu His Val Ala Glu
65          70          75          80
Ile Val Gly Arg Gln Gly Arg Ser Arg Arg Asp Gly Glu Leu Asp Pro
          85          90          95
Ser Gly Ile Ser Pro Asp Asp Phe Ser Gly Ile Leu Gly Phe Gly Ser
          100          105          110
Gly Arg Leu Gln Ser Leu Gly Glu Gly Gln Ala Ala Asn Gly Leu Phe
          115          120          125
Leu Glu Arg Leu Ala Gly Gly Ile Arg Cys Pro Ala Arg Gly Ala Ala
130          135          140
Arg Gly Cys Lys Ile Lys Ala Leu Arg Ala Lys Thr Asn Thr Tyr Ile
145          150          155          160
Lys Thr Pro Val Arg Gly Glu Glu Pro Val Phe Val Val Thr Gly Arg
          165          170          175
Lys Glu Asp Val Ala Met Ala Arg Arg Glu Ile Ile Ser Ala Ala Glu
          180          185          190
His Phe Ser Met Ile Arg Ala Ser Arg Asn Lys Asn Thr Ala Leu Asn
195          200          205
Gly Ala Val Pro Gly Pro Pro Asn Leu Pro Gly Gln Thr Thr Ile Gln
210          215          220
Val Arg Val Pro Tyr Arg Val Val Gly Leu Val Val Gly Pro Lys Gly
225          230          235          240
Ala Thr Ile Lys Arg Ile Gln Gln Gln Thr His Thr Tyr Ile Val Thr
          245          250          255
Pro Ser Arg Asp Lys Glu Pro Val Phe Glu Val Thr Gly Met Pro Glu
          260          265          270
Asn Val Asp Arg Ala Arg Glu Glu Ile Glu Ala His Ile Ala Leu Arg
275          280          285
Thr Gly Gly Ile Ile Glu Leu Thr Asp Glu Asn Asp Phe His Ala Asn
290          295          300
Gly Thr Asp Val Gly Phe Asp Leu His His Gly Ser Gly Gly Ala Ser
305          310          315          320

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Thr Asp Ser Tyr Phe Gly Gly Gly Thr Ser Ser Ser Ala Ala Ala Thr  
 325 330 335  
 Gln Arg Leu Ala Asp Tyr Ser Pro Pro Ser Pro Ala Leu Ser Phe Ala  
 340 345 350  
 His Asn Gly Asn Asn Asn Asn Gly Asn Gly Tyr Thr Tyr Thr Ala  
 355 360 365  
 Gly Gly Glu Ala Ser Val Pro Ser Pro Asp Gly Cys Pro Glu Leu Gln  
 370 375 380  
 Pro Thr Phe Asp Pro Ala Pro Ala Pro Pro Pro Gly Ala Pro Leu Ile  
 385 390 395 400  
 Trp Ala Gln Phe Glu Arg Ser Pro Gly Gly Gly Pro Ala Ala Pro Val  
 405 410 415  
 Ser Ser Ser Cys Ser Ser Ser Ala Ser Ser Ser Ala Ser Ser Ser  
 420 425 430  
 Val Val Phe Pro Gly Gly Gly Ala Ser Ala Pro Ser Asn Ala Asn Leu  
 435 440 445  
 Gly Leu Leu Val His Arg Arg Leu His Pro Gly Thr Ser Cys Pro Arg  
 450 455 460  
 Leu Ser Pro Pro Leu His Met Ala Pro Gly Ala Gly Glu His His Leu  
 465 470 475 480  
 Ala Arg Arg Val Arg Ser Asp Pro Gly Gly Gly Gly Leu Ala Tyr Ala  
 485 490 495  
 Ala Tyr Ala Asn Gly Leu Gly Ala Gln Leu Pro Gly Leu Gln Pro Ser  
 500 505 510  
 Asp Thr Ser Gly Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser  
 515 520 525  
 Ser Ser Ser Ser Gly Leu Arg Arg Lys Gly Ser Arg Asp Cys Ser Val  
 530 535 540  
 Cys Phe Glu Ser Glu Val Ile Ala Ala Leu Val Pro Cys Gly His Asn  
 545 550 555 560  
 Leu Phe Cys Met Glu Cys Ala Asn Arg Ile Cys Glu Lys Ser Glu Pro  
 565 570 575  
 Glu Cys Pro Val Cys His Thr Ala Val Thr Gln Ala Ile Arg Ile Phe  
 580 585 590  
 Ser

<210> 73  
 <211> 472  
 <212> PRT  
 <213> Homo sapiens

<400> 73  
 Met Pro Ser Ser Leu Phe Ala Asp Leu Glu Arg Asn Gly Ser Gly Gly  
 1 5 10 15  
 Gly Gly Gly Gly Ser Ser Gly Gly Gly Glu Thr Leu Asp Asp Gln Arg  
 20 25 30  
 Ala Leu Gln Leu Ala Leu Asp Gln Leu Ser Leu Leu Gly Leu Asp Ser  
 35 40 45  
 Asp Glu Gly Ala Ser Leu Tyr Asp Ser Glu Pro Arg Lys Lys Ser Val  
 50 55 60  
 Asn Met Thr Glu Cys Val Pro Val Pro Ser Ser Glu His Val Ala Glu  
 65 70 75 80  
 Ile Val Gly Arg Gln Gly Cys Lys Ile Lys Ala Leu Arg Ala Lys Thr  
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 Thr Thr Ile Gln Val Arg Val Pro Tyr Arg Val Val Gly Leu Val Val  
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&lt;210&gt; 74

&lt;211&gt; 607

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 74

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Val Val Ile Gln Ala Lys Asp Met Gly Gly His Met Gly Gly Leu Ser
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 <213> Homo sapiens

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Leu Asp Ser Pro Ala Ser Pro Ile Arg Tyr Ser Ile Leu Pro His Ser
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Asp Pro Glu Arg Cys Phe Ser Ile Gln Pro Glu Glu Gly Thr Ile His
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Thr Ala Ala Pro Leu Asp Arg Glu Ala Arg Ala Trp His Asn Leu Thr
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Val Leu Ala Thr Glu Leu Asp Ser Ser Ala Gln Ala Ser Arg Val Gln
          450          455          460
Val Ala Ile Gln Thr Leu Asp Glu Asn Asp Asn Ala Pro Gln Leu Ala
465          470          475          480
Glu Pro Tyr Asp Thr Phe Val Cys Asp Ser Ala Ala Pro Gly Gln Leu
          485          490          495
Ile Gln Val Ile Arg Ala Leu Asp Arg Asp Glu Val Gly Asn Ser Ser
          500          505          510
His Val Ser Phe Gln Gly Pro Leu Gly Pro Asp Ala Asn Phe Thr Val
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Thr Cys Val Gly Ala Leu Leu Ala Leu Val Val Leu Phe Val Ala Leu
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Thr Glu Ala Phe Asp Ile Thr Ala Leu Gln Asn Pro Asp Gly Ala Ala
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705          710          715          720
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 <212> PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

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Ser	Asp	Pro	Ser	Gln	Leu	Asn	Leu	Tyr	Met	Arg	Phe	Glu	Asp	Glu	Ser	50	55	60	
Phe	Asp	Arg	Leu	Leu	Trp	Ser	Ala	Lys	Glu	Pro	Ser	Asp	Ser	Trp	Leu	65	70	75	80
Ile	Ala	Ser	Leu	Asp	Leu	Gln	Asn	Ser	Ser	Lys	Lys	Phe	Lys	Ile	Leu	85	90	95	
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Tyr	Ile	Phe	Glu	Glu	Asn	His	Val	Val	Gln	Glu	Lys	Ile	Trp	Ser	Val	385	390	395	400
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 180 185 190  
 Gly Gly Gly Ser Ile Arg Asn Val His Ser Ile Leu Pro Gln Asp His  
 195 200 205  
 Thr Phe Lys Ser Glu Leu Gly His Tyr Met Tyr Val Asp Ser Val Tyr  
 210 215 220

Val	Lys	His	Phe	Gln	Glu	Val	Ala	Gln	Leu	Ile	Ser	Pro	Leu	Thr	Thr	225	230	235	240
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Gly	Thr	Gly	Leu	Leu	Ser	Val	Tyr	Leu	Lys	Lys	Glu	Glu	Asp	Ser	Glu	595	600	605	
Glu	Ser	Leu	Leu	Trp	Arg	Arg	Arg	Gly	Glu	Gln	Ser	Ile	Ser	Trp	Leu	610	615	620	
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Glu	Ala	Ile	Arg	Gly	Val	Ser	Ile	Arg	Ser	Asp	Ile	Ala	Ile	Asp	Asp	645	650	655	
Val	Lys	Phe	Gln	Ala	Gly	Pro	Cys	Gly	Glu	Met	Glu	Asp	Thr	Thr	Gln	660	665	670	
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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/13360

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C07H 21/04; C12P 21/06; C12N 9/00, 1/20, 15/00

US CL : 435/69.1, 183, 252.2, 320.1; 536/23.2

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 183, 252.2, 320.1; 536/23.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
BIOSIS, CAPLUS, MEDLINE, EMBASE, GENBANK, SCISEARCH**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	CARNINCI, P et al. Normalization and subtraction of cap-trapper-selected cDNAs to prepare full-length cDNA libraries for rapid discovery of new genes, <i>Genome Res.</i> , October 2000, Vol.10, No.10, pages 1617-1630, see entire article.	1-7
A, P	WO 00/55350 A1 (HUMAN GENOME SCIENCES, INC.) 21 September 2000 (21-9-00).	1-7
A	WO 95/30428 A1 (HUMAN GENOME SCIENCES, INC.) 16 November 1995 (11-16-95).	1-7
A	US 5,830,744 A (ROSEN et al.) 03 November 1998 (11-03-98).	1-7

☐ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"I"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 07 JULY 2001	Date of mailing of the international search report 02 AUG 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20531 Facsimile No. (703) 305-3230	Authorized Officer MANUNATH RAO Telephone No. (703) 308-0196

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/13860

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-7, SEQ ID NO:1 and 40

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/13360

### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

- 1) Polynucleotide sequences with SEQ ID NOs 1 through 39.
- 2) Polypeptide sequences with SEQ ID NOs: 40-78.

The following claims are generic: Claims 1-7

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the above polynucleotide and polypeptide sequences are patentably distinct from each other as they have different structure and function.